MAY 9 1939
MEDICAL LIBRARY

JOURNAL OF NEUROPHYSIOLOGY

J. NEUROPHYSIOL.

EDITORIAL BOARD

J. G. DUSSER de BARENNE
J. F. FULTON R. W. GERARD

ADVISORY BOARD

E. D. ADRIAN (Cambridge)
PERCIVAL BAILEY (Chicago)
PHILIP BARD (Baltimore)
G. H. BISHOP (St. Louis)
F. BREMER (Brussels)
DETLEV W. BRONK (Philadelphia)
E. VON BRÜCKE (Boston)
STANLEY COBB (Boston)
HALLOWELL DAVIS (Boston)
U. EBBECKE (Bonn)
J. C. ECCLES (Sydney)
JOSEPH ERLANGER (St. Louis)
WALLACE O. FENN (Rochester)
ALEXANDER FORBES (Boston)
H. S. GASSER (New York)
RAGNAR GRANIT (Helsingfors)
W. R. HESS (Zürich)
MARION HINES (Baltimore)
DAVENPORT HOOKER (Pittsburgh)
R. LORENTE DE NÓ (New York)
WILDER PENFIELD (Montreal)
H. PIÉRON (Paris)
S. W. RANSON (Chicago)
C. S. SHERRINGTON (Ipswich)

MAY 1939

VOL. II ISSUED BI-MONTHLY NO. 3

PUBLISHED BY CHARLES C THOMAS
220 EAST MONROE STREET, SPRINGFIELD, ILLINOIS, U.S.A.

JOURNAL OF NEUROPHYSIOLOGY

SCOPE: The aim of the *Journal of Neurophysiology* is to provide a channel for *prompt* publication of original contributions on the functions of the nervous system, peripheral and central. Materials submitted may include any phase of the subject amenable to experimental analysis; papers on pure morphology or neuropathology are not acceptable. Clinical, psychological and zoological studies will be considered only if primarily experimental in character.

MANUSCRIPTS: Manuscripts should be addressed to THE EDITORS, JOURNAL OF NEUROPHYSIOLOGY, 333 Cedar Street, New Haven, Connecticut, U.S.A. Papers should be concise and submitted in typewritten form, preferably in triple space, with tabular matter and passages for small print in double space and on separate sheets. All materials should be mailed flat. A brief summary should be included.

REFERENCES: Citations of literature, in alphabetical order and typed on a separate sheet, should include names and initial(s) of the author(s) with *full title* and full pagination of the book or paper. Citations of books and monographs should include also publisher, place and year. Names of journals should be abbreviated in accordance with the system used in *A world list of scientific periodicals published in the years 1900–1933* (Oxford University Press, 1934). For other details of form see the references in this number. References may be cited in the text by year or by elevated numerals.

A Style Book for the *Journal* will be supplied free of charge to contributors; additional copies may be purchased at 25 cents each.

COSTS CHARGEABLE TO AUTHORS—*Illustrations*: The allowance for free illustrations varies with the length of the paper and the character of the illustrative matter, but not more than four 3×3.5 inch half-tones (or their equivalent in area) will be allowed free to any contributor. When a paper has been accepted for publication, authors will be notified promptly of any charges for illustrations in excess of the free allowance. These will be charged to the author at a rate of approximately $5.00 for a 3×3.5 inch (7.6×8.9 cm.) half-tone and at a somewhat lower rate for zinc cuts. All illustrations, especially photographs, should be sharp and clear and submitted ready for reproduction, *i.e.*, with lettering, mounting and arrangements of figures completed.

Special typography. Tables, mathematical and chemical formulae and also text set up in small print (8 point) in excess of 10 per cent of composition costs are chargeable to the author.

Proof corrections. Corrections in galley proof will be allowed without charge up to 5 per cent of the original cost of composition of 10 point type. The cost of changes in page proof, if made by the author, will be borne by him. *Page proof* will be submitted to authors only when special questions arise. Manuscripts and figures will be returned after the editorial office has corrected page proof.

Reprints. Twenty-five reprints of each paper will be supplied without charge; larger numbers can be purchased at cost; delivery will be prompt. Reprints should be ordered on forms accompanying the galley proof and returned with it to the Editorial Office.

SUBSCRIPTIONS: The subscription rate for the volume of six bi-monthly issues is $6.00 in the United States, Canada and Latin America, and $6.50 in other countries. It is payable in advance to the publisher: CHARLES C THOMAS, 220 East Monroe Street, Springfield, Illinois, U.S.A.

Entered as second-class matter February 13, 1939, at the postoffice at Springfield, Illinois, and Menasha, Wisconsin under the Act of March 3, 1879

COPYRIGHT, 1939 BY CHARLES C THOMAS

THE CONDITIONED REFLEX OF BLINKING

G. MARTINO

Istituto di Fisiologia Umana R. Università di Messina, Sicily

(Received for publication November 10, 1938)

FOR SEVERAL years work has been carried on in this laboratory on a particular conditioned motor reflex whose elaboration it has been possible to obtain in the dog—the reflex of blinking. The observations so far made have been published in various Italian journals, and since they allow of certain conclusions of a general nature, particularly in regard to the intimate mechanism of conditioned reactions, it is desirable to describe them here.

The unconditioned (innate or original) reflex of blinking, in the dog, consists in a rapid contraction of m. orbicularis oculi in response to the action of an adequate stimulus on a reflexogenous cutaneous area (in the homolateral half of the face). It is under the control of a cortical motor centre of the gyrus sigmoideus (whose activity is of a reflex nature), and a state of activity in this cortical centre, made manifest by the contraction of the orbicularis oculi on the opposite side, is provoked by centripetal impulses which start from this well-defined reflexogenous cutaneous area. Electric stimulation of this area invariably provokes in all dogs the reflex contraction of the orbicularis oculi, and frequently repeated association of indifferent sensory stimuli (of various kinds) with the innate reflex has permitted the development of *conditioned reflexes of blinking*.

The analysis of these has given interesting results on the problem of the intimate mechanism of associative reactions. According to the concept of Pavlov, the development of conditioned reflexes is attained by substitution in the arc of the congenital reflex of the unconditioned afferent path with a new (conditioned) centripetal path. Only the last segment of the arc would remain unchanged—the part which conveys the impulses to the peripheral effector organ. We found that after stovainisation of the reflexogenous cutaneous area of the congenital arc, the conditioned stimuli—luminous[1] or auditory[2]—lost their previously acquired capacity of exciting the reaction of blinking. The reflexogenous area of the unconditioned arc is therefore an essential part in the mechanism of the conditioned reflex; in other words, the persistence and integrity of the congenital afferent path represents an *essential condition* for the manifestation of associative reactions. It is not then by the replacement of the common centripetal path by the conditioned afferent one that "action at a distance" (*Fernwirkung*) of conditional exciters becomes possible.

We thought that this action might consist in the facilitation (*Bahnung*) of the congenital reflex. In this case the capacity of the conditioned stimulus to provoke the active state of the reflex centre would be only apparent. In reality that stimulus would only cause an increase in the excitability of the centre, and the active state, in the last analysis, would always be induced, in the associative reaction as in the congenital, by unconditioned afferent stimuli.

In order to test the validity of this hypothesis we studied the activity of

the motor centre during the action of conditioned stimuli in dogs trained to conditioned blinking reflexes.[3] We found an increase in its faradic excitability and observed, after central treatment with strychnine, that provocations of reflex clonus and of reflex epileptic forms by peripheral stimuli were facilitated.*

Another proof of the effect of the conditioned stimuli on the excitability of the reflex centre is furnished by the following observation: during the elaboration of an associative reflex the threshold of the unconditioned stimulus is lowered progressively as the efficacy of the conditioned signals progressively increases. Thus an unconditioned stimulus, insufficient in itself to provoke the reflex contraction of the m. orbicularis oculi, becomes capable of doing so if preceded by a conditioned signal, even though the latter by itself is insufficient to cause the reaction of blinking.[4]

Finally, a further (indirect) demonstration of these effects of the sensory associative stimulus on the excitability of the reflex centre is found in the following experimental observations: In this Institute it had been shown previously that a functional connection exists between a given point of the occipital cortex (visual area) of the dog and the motor centre of the m. orbicularis oculi of the same hemisphere, so that the reflex activity of the latter centre is facilitated by direct circumscribed strychninisation of a point in the occipital cortex.[5] Two distinct conditioned reflexes of blinking were then elaborated in a dog in response to luminous stimuli—with the left eye to red light, and the right to violet. After the application of strychnine to the occipital cortex of the left hemisphere violet light showed the power of provoking clonus of the right m. orbicularis oculi followed by generalized attacks of epileptic nature (arising from this muscle). On the other hand no effect was obtained by stimulation with red light. After strychninisation of the occipital cortex of the right hemisphere we obtained on the contrary clonic twitches of the left orbicularis—and subsequent epileptic attacks—under the action of red light but not under that of violet.[6]

This therefore is the effective mechanism of the associative reactions: the conditioned impressions from the sensory cortex bombard the motor centre and augment its excitability while its active state is still induced by the centripetal impulses congenitally destined to this purpose, that is, by those which start from the reflexogenous region of the unconditioned arc. "It cannot be denied, indeed it is necessary to recognize, that centripetal impulses are continually starting from the peripheral reflexogenous zones in response to the influence of numerous stimuli. Such impulses are normally inactive and therefore in ordinary circumstances the reaction—motor or secretory—does not take place in the absence of the adequate stimulus, natural or artificial, but this is dependent on the degree of excitability of the reflex centre. If this central excitability is increased beyond certain limits, then these subliminal af-

* Diminution of chronaxie—*i.e.*, increase of excitability—in the reflex centre under the action of conditioned stimuli has been observed by Chauchard and Drabovitch (*C. R. Soc. Biol., Paris*, 1936, *2*: 67).

ferent impulses, usually inactive, may prove themselves sufficient to excite the activity of the reflex centre."[7]

On account of the symmetrical bilateral organization of the cortical centres the reflex of blinking makes possible a rigorous comparison between the effects of different conditioned stimuli.[8] In the same animal it is, in fact, possible to obtain the simultaneous elaboration of *two different* conditioned reflexes of blinking. This, obviously, is not possible for the reflex of the salivary secretion. The comparison between the effects produced by different stimuli on different animals, or even on the same animal at different times, cannot furnish data of much value because of the importance of the individuality of the animal and of numerous other factors in the elaboration and extinction of associative reflexes.*

In agreement with the observations of Pavlov on the conditioned reflexes of salivary secretion we have found that luminous stimuli are less effective than sonorous in the elaboration of the associative reflex. Moreover the reflexes elaborated by means of sonorous signals have shown a greater resistance to the phenomenon of extinction.

In other experiments carried out on a dog trained to a double conditioned reflex of blinking by luminous signals (violet light for one eye, red light for the other) it was possible to recognize certain effects, related to the *quality* of the luminous conditioned stimulus, on the processes of facilitation and inhibition. In particular, red light ($\lambda = 7200 - 6000$ Å) showed itself less effective than violet ($\lambda = 5500 - 4250$ Å) in the elaboration of the associative reflex, and the reflex was less resistant to extinction in the former than in the latter case. Since the greater or less effectiveness of the conditioned agent depends on the greater or less sensitiveness of the sensory analyser (Pavlov[9]) this result shows that the optical analyser of the dog is more sensitive to rays of wave length corresponding to our violet light than to those of wave length corresponding to our red light. This behavior is similar to that of the optical analyser in man.[10] Violet light showed itself more effective than red in restoring an associative reaction which had been extinguished. Moreover in the case of red light the impulses showed a greater tendency to irradiation; in that of violet light, to concentration. Pavlov considered that the tendency of impulses to irradiate or to concentrate varies according to the energy of the sensory agent; stronger impulses tend more readily to concentration, while the weaker are generally more disposed to irradiation. Our observation therefore constitutes a further

---

* Pavlov wrote concerning the phenomenon of "internal inhibition (extinction)": "It is necessary first of all to mention the influence of the individuality of the animals. In some, other things being equal, the conditioned reflexes are rapidly extinguished, in others very slowly. This fact is closely connected with the general character of the nervous system of the animal. In nervous and excitable dogs the reflexes are usually slowly extinguished; in quiet and calm dogs they are extinguished rapidly. The degree of development of the reflex also plays its part. The younger and the weaker it is, the more rapidly it is extinguished, and vice-versa. The intensity of the absolute reflex with whose aid the conditioned has been formed exercises a well-defined influence on the rapidity of extinction . . . " (*Leçons sur l'activité du cortex cérébral*. A Legrand. Paris, 1929, p. 52).

proof of the difference of energy of the two luminous stimuli of different quality.

We have also obtained the contemporaneous elaboration of two conditioned reflexes by means of sound signals of different quality:[4] blinking of the left eye to the note mi^7 (5520 vibrations) and of the right to the note fa^7 (5568 vibrations). Although the interval between the two notes is hardly a semitone, the dog quickly learned to distinguish between the two signals so that in a short time absolutely correct conditioned responses were obtained. The note mi^7 showed itself more effective than fa^7 in the elaboration of this conditioned reflex and the reflex produced was more resistant to extinction.

In the course of the experiment we observed on several occasions typical phenomena of external inhibition in which the established associative reflex became weaker, or even completely vanished, as a result of noises accidentally penetrating into the laboratory. In such cases we observed sometimes a marked diminution in the *power of discrimination*, so that the dog responded, for example, to the signal mi^7 by a contraction of the right orbicularis (instead of the left) or to fa^7 by the left orbicularis (instead of the right). On some rare occasions a similar diminution of discriminative power was observed as a result of fatigue, at the end of an unduly prolonged trial. These are inhibitory effects, which may logically be attributed to a relaxing of attention. Other observations on the processes of inhibition, or disinhibition, etc., are in agreement with Pavlov's results on the associative reflexes of salivary secretion.

It is appropriate to mention here the recent interesting experiments of Gantt and his collaborators on the anatomical structures engaged in the elaboration of the conditioned reflex. They have shown that in the elaboration of an associative reflex the external conditioned stimulus may be replaced by artificial stimulation (faradic) of various parts of the central nervous system.[11] This constitutes an indirect confirmation of my views on the intimate mechanism of conditioned reactions: a proof that no necessity exists for a special arc of the associative reflex substantially different from the congenital one. We could not otherwise explain the effects of the so-called "intra-neural conditioning" (Gantt) except by invoking the phenomenon of *Bahnung*. In no other way save by increase in the excitability of the reflex centre could the artificial stimulation of the cerebellum or of the cerebral cortex or of the posterior spinal roots elicit the reaction which depends upon that centre. Analogous processes of facilitation ("sekundäre Bahnung" of the German investigators) have long been known. A clear distinction between the factors which determine the active state of the reflex centre and those which increase its excitability is therefore an indispensable condition for a correct understanding of the mechanism of associative reflexes.

REFERENCES

1. MARTINO, G., and ALIBRANDI, A. Analisi di un particolare riflesso condizionato (dell' ammiccamento), nel cane. *Boll. Soc. ital. sper.*, 1936, *11*: 763–764.
2. ALIBRANDI, A. Nuova conferma sperimentale per la necessaria partecipazione della via afferente congenita al meccanismo dei riflessi condizionati. *R. C. Accad. Lincei*, 1938, *27*: 479–481.

3. MARTINO, G., and ALIBRANDI, A. L'attività riflessa del centri sensitivomotori corticali sotto l'azione di stimoli condizionati. *Arch. Fisiol.*, 1937, *37:* 533–538.
4. MARTINO, G., and ALIBRANDI, A. Nuove osservazioni sui riflessi condizionati dell' ammiccamento (per stimoli acustici). *R. C. Accad. Lincei*, 1938, *27:* 168–171.
5. FULCHIGNONI, E. Sul meccanismo dell' epilessia sperimentale riflessa per stimoli luminosi. *R. C. Accad. Lincei*, 1938, *27:* 122–125.
6. MARTINO, G., and FULCHIGNONI, E. Über die Bedeutung bedingter Reize (für den Bahnungsprozess) bei der durch Strychninisierung der occipitalen Rinde reflektorisch erzeugte Epilepsie. *Pflüg. Arch. ges. Physiol.*, 1938, *240:* 212–220.
Il fenomeno dell' agevolazione nell' epilessia riflessa da stricninizzazione occipitale, sotto l'azione di stimoli luminosi condizionati. *R. C. Accad. Lincei*, 1938, *27:* 125–128.
7. MARTINO, G. Necessità della ordinaria via afferente, costante ed insostituibile, nel meccanismo del riflesso associativo. *Atti. R. Accad. Peloritana*, 1936, *38:* 67–74.
8. MARTINO, G., and ALIBRANDI, A. L'agevolazione e l'inibizione in rapporto alla qualità dello stimolo luminoso, nel riflesso condizionato dell' ammiccamento. *Arch. Fisiol.*, 1938, *38:* 200–219.
9. PAVLOV, J. P. *Leçons sur l'activité du cortex cérébral*. Paris, LeGrand, 1929.
10. MARTINO, G. Sulla sensibilità dell'analizzatore ottico del cane per raggi luminosi di diversa lunghezza d'onda. *Atti. R. Accad. Peloritana*, 1938, *40:* 89–94.
11. GANTT, W. H. Kongressbericht II des XVI Intern. Physiologenkongresses, 1938, p. 116.

SUR UN PHÉNOMENE DE FACILITATION RÉTROACTIVE DANS L'ÉXCITATION ÉLECTRIQUE DE BRANCHES NERVEUSES CUTANÉES (SENSIBILITÉ TACTILE)

H. PIÉRON ET J. SEGAL
Collège de France, Paris, France

(Received for publication November 25, 1938)

INTRODUCTION

AU COURS de recherches sur les processus d'excitation de la sensibilité tactile, par stimulation électrique, au moyen de décharges de condensateurs, d'une branche cutanée sensitive (un rameau de la branche latérale cutanée externe du médian, à la base de la première phalange), certains faits d'allure paradoxale ont été mis en évidence, faits signalés dans la note préliminaire que nous avons publiée sur ces recherches.[1] Ils consistent essentiellement en un accroissement de l'efficacité d'un choc sous-liminaire sous l'influence d'un choc consécutif, dans une assez grande marge d'intervalles, et en un raccourcissement du temps de réaction à une stimulation par un choc, du fait de la production consécutive d'un second choc, dans les limites d'une marge d'étendue analogue.

Ces faits posent un problème dont la solution doit impliquer certaines conséquences au point de vue des processus de réception sensorielle et de leur mécanisme cérébral. Nous indiquerons tout d'abord la méthode et la technique des recherches, puis les données générales obtenues, avant de décrire les phénomènes de facilitation rétroactive observés et d'en discuter l'interprétation.

I. METHODE ET TECHNIQUE EXPERIMENTALE

Après divers tâtonnements relatifs à des stimulations électriques de plusieurs branches nerveuses, nous avons choisi un rameau terminal uniquement sensitif et accessible dans une région où l'on ne risque plus d'exciter des muscles et de provoquer des contractions avec leurs répercussions sensitives.

A la base de la première phalange du médius, en tâtonnant latéralement avec une électrode de Bourguignon, on arrive à déterminer un point où les stimulations d'un rameau superficiel, sur le territoire du médian, provoquent des sensations de choc tactile au niveau de la 2 ème phalange dans une région latérale, près de l'articulation proximale. Avec des décharges de condensateur assez brèves, on ne provoque d'impression douloureuse que sous des voltages assez élevés, au triple environ du voltage liminaire quand la durée de décharge est égale à la chronaxie. Nous avons donc utilisé systématiquement des durées de décharge égales à la chronaxie, déterminée chaque fois au préalable, ce qui nous a permis d'obtenir des sensations exclusivement tactiles, pour une marge assez grande, relativement, des intensités de stimulation. En utilisant, ainsi, des décharges de condensateurs, il était possible de réaliser des stimulations multiples, de durée définie, en réglant leur nombre et leur intervalle grâce à un dispositif contacteur constitué par un cylindre tournant.

Pour réaliser les voltages élevés nécessaires, atteignant plusieurs centaines de volts, nous avons dû nous servir de piles sèches avec réglage direct des tensions par le jeu des fiches (échelons de 1.5 volt). Un potentiomètre à faible résistance aurait vite mis les piles hors service et une grande résistance aurait rendu trop lente la charge des condensateurs qui devait être très rapidement effectuée. Toutefois un potentiomètre de faible résistance a été quelquefois utilisé pour une stimulation additive dans la mesure des seuils différentiels. Le dispositif de stimulation est conforme au schéma classique.

Circuit de décharge. Le condensateur variable C (de la figure 1) est branché successivement sur la pile P_1 et sur le circuit de décharge, qui comporte une résistance de 25,000 ohms en série avec le sujet, une autre de 7,000 ohms en parallèle avec lui, et une troisième de 18,000 ohms en série avec le condensateur. Dans ces conditions 0.001μF correspond à une durée de décharge d'environ 0.009 msec. Pour déterminer la *rhéobase*, on court-circuitait au moyen du manipulateur M_1. Avec le manipulateur M_2 on pouvait brancher à volonté dans le circuit une pile P_2 apportant un voltage supplémentaire déterminé, quand on faisait varier l'intensité de stimulation au cours des chocs consécutifs (et, dans certains cas, un potentiomètre à faible résistance pouvait être branché en P_2).

Relais de commande. Normalement, les stimulations étaient assurées par des contacts au niveau du relais R_1 spécialement construit sur le type des signaux de Després, et capable de suivre des fréquences d'intermittences s'élevant jusqu'à 400 par seconde, grâce à sa très faible inertie, et à l'absence de fréquence propre, ce qui permettait, au moyen du contacteur, d'imposer des rythmes de stimulations brèves définis en nombre et en fréquence.

Contacteur. Le contacteur consistait en un cylindre métallique recouvert d'un papier calque

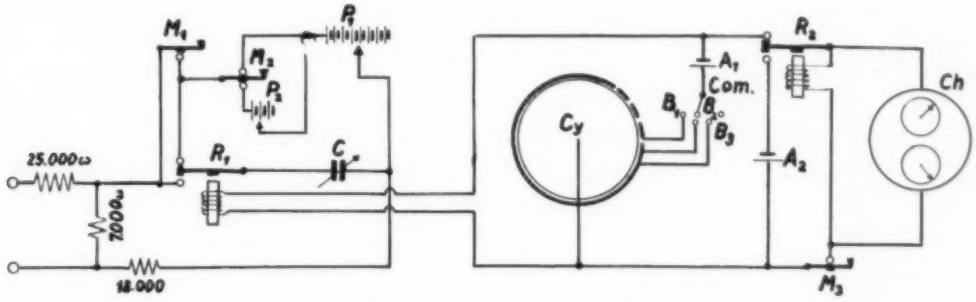

FIG. 1. Schéma du dispositif utilisé pour la stimulation par décharges de condensateurs uniques ou répétées à intervalles variables, et pour la détermination des temps de réaction (signification des lettres et explication dans le texte).

dans lequel étaient découpées des ouvertures formant des séries linéaires parallèles, de nombre et d'intervalle déterminés.

Un balai frottant sur la surface, et fermant un circuit, au passage de chaque ouverture d'une série au niveau de laquelle il était placé sur son support, permettait l'envoi des décharges de condensateurs. Le circuit, commandant le relais, comportait un accumulateur A_1, le balai, la masse du cylindre, et le bobinage du relais. La durée exacte du contact, assurant, par la manoeuvre du relais, la décharge du condensateur, n'avait pas d'importance. Dans l'intervalle de deux contacts, le condensateur était rechargé.

En plaçant sur support, côte à côte, trois balais B_1, B_2, B_3, chacun devant une série de perforations du papier du cylindre, on pouvait, par le jeu du commutateur, Com, changer la série des stimulations, comparer par exemple 1 choc unique et 2 chocs, ou 2 chocs séparés par un certain intervalle et 2 chocs semblables séparés par un intervalle plus petit ou plus grand, etc.

Dispositif des temps de réaction. Pour la mesure des temps de réaction, le balai, en réalisant le contact par l'ouverture du papier, commandait, outre le relais R_1 à retour spontané (commandé par un ressort), un relais R_2 à déclenchement spontanément irréversible, et branchant un chronoscope de Hipp sur le circuit de l'accumulateur A_2; la marche de l'aiguille, dont le départ était déclenché dès la commande du relais par l'accumulateur A_1 avant la constitution du circuit de A_2, était assurée jusqu'à ce que le sujet réalisât l'arrêt, par sa réaction, en interrompant le circuit par jeu du manipulateur M_3 (pressant sur le bouton d'une clef de Morse), provoquant en outre le retour du relais R_2 en position de départ et prêt ainsi pour une nouvelle mesure de temps de réaction.

Electrodes. Les électrodes, du type impolarisable zinc—sulfate de zinc, comportaient une anode indifférente constituée par une large plaque de zinc entourant le poignet avec, interposé, du coton imbibé de la solution de sulfate de zinc, une bande élastique maintenant la plaque, et une cathode active, spécialement construite pour l'application sur le doigt (médius gauche, face externe); celle-ci était faite d'un petit bloc cylindrique d'ébonite avec noyau de zinc, et, dans une cavité rejoignant le noyau, un bouchon de coton imbibé, la

base du bloc, assez large, épousant la forme du doigt; mais la partie active de l'électrode restait limitée à une surface de petit diamètre (environ 3 mm.). Avec fixation par un élastique à tenseur, une telle électrode reste bien en place même au cours des mouvements du doigt, et, grâce à l'étanchéité, le desséchement est très lent, et l'on peut opérer pendant plus d'une heure sans toucher à l'électrode.

Le sujet était placé dans une pièce, l'expérimentateur dans une autre (en sorte que les manipulations n'étaient point vues et que le déclic du chronoscope n'était pas entendu). Une signalisation lumineuse permettait les communications entre l'expérimentateur et le sujet.

II. Données Generales sur les Faits Observés

Une décharge très brève de condensateur engendre une sensation tactile de choc dont on a toutes raisons de penser qu'elle correspond à l'envoi d'une influx unique, sans qu'il y ait nécessité d'une itération. Dès lors la mesure d'une chronaxie sensitive véritable peut être envisagée comme correcte. Il y a probabilité en effet que, dans la détermination de la rhéobase, donnant bien au seuil une sensation tactile de fermeture, ce sont les mêmes fibres qui sont mises en jeu.

Avec 8 sujets et 28 déterminations, la valeur moyenne de la chronaxie a été de 0,38 msec. Mais, avec des décharges répétées, on a un abaissement du seuil. Le voltage liminaire, très légèrement abaissé (de l'ordre de 1 per cent) pour un double choc avec un intervalle de 0,80 sec. est diminué de près de 10 pour cent lorsque l'intervalle des deux chocs est de l'ordre des centièmes de seconde. Le voltage liminaire, pour des stimulations intermittentes continues (au rythme de 25 à la seconde) est abaissé d'environ 13 per cent, l'intégration portant sur 4 stimulations successives au moins. Avec l'augmentation du voltage (en durée fixe) l'intensité du choc s'accroît, et la sensibilité différentielle est fine (pouvant atteindre, comme optimum, moins de 1 per cent chez certains sujets). La variation du seuil différentiel relatif avec le niveau d'intensité a une allure assez complexe.

Pour des stimulations rythmées, on a une sensation de type vibratoire, un "flicker" tactile, avec tendance à la fusion vers 200 par seconde pour des intensités faibles, proches du seuil. Aux intensités un peu élevées, la stimulation intermittente met en jeu beaucoup plus tôt la sensibilité algique que les stimulations isolées, d'où un picotement qui rend difficile la détermination de la fréquence critique de fusion tactile. La sensibilité différentielle à la fréquence, pour une stimulation intermittente, dans ces conditions, s'est montrée assez grossière, des variations, pour être perçues (autour d'une fréquence de 50 à la seconde) devant atteindre un taux de 30 à 50 per cent. Dans la stimulation intermittente prolongée. l'adaptation se produit, avec extinction totale d'autant plus précoce que le niveau d'intensité est plus las, 5 secondes aux environs du seuil, 35 secondes pour un voltage 1,25 fois supérieur. Ce temps d'adaptation diminue progressivement quand on reprend, après un court repos, les stimulations rythmées au même niveau d'intensité.

III. La Facilitation Rétroactive Par Double Choc

Au cours de l'étude des processus de sommation, des séries de déterminations furent faites, chez divers sujets, du voltage liminaire par application

d'un choc unique de durée chronaxique, ou de deux chocs consécutifs, de cette même durée, séparés par un intervalle variable, l'efficacité de la sommation se manifestant encore pour un intervalle de 0,4 sec., mais non pour un intervalle de 0,8 chez la plupart des sujets.

On cherchait alternativement, à plusieurs reprises, le seuil du choc unique et du double choc. Voici, par exemple, des valeurs obtenues chez un sujet, avec un intervalle de 20 msec. (durée chronaxique de décharge de 0,48 msec.):

Nombre de chocs:	1	2	1	2	1	2	1
Voltage liminaire:	129	102	126	88	124,5	99	123

Avec un intervalle de 166 msec., on obtient chez le même sujet:

Nombre de chocs:	1	2	1	2	1
Voltage liminaire:	135	126	133,5	124,5	130,5

Or, en appliquant le double choc avec le voltage correspondant au seuil du choc unique, le sujet, pour cet intervalle de 166 msec, percevait nettement les deux chocs consécutifs, mais, en abaissant le voltage, continuait à percevoir les deux chocs et cela jusqu'au voltage liminaire. Ainsi à 126 volts, en appliquant les deux chocs de condensateurs consécutifs, il y a perception de deux chocs mécaniques; avec ce voltage, le choc électrique unique est inefficace et ne donne pas naissance à une sensation; en augmentant le voltage jusqu'à 135 volts par unités d'l, 5 v., on obtient chaque fois, avec ce double choc électrique, la perception de deux chocs mécaniques mais avec un seul choc électrique, aucune sensation, tant qu'on n'a pas atteint 133,5 volts,—le choc unique commençant alors à être efficace (au lieu de 135 v., préalablement). Pour des intervalles plus courts, les deux chocs mécaniques étaient aussi perçus avec des voltages inférieurs au seuil d'efficacité du choc électrique unique, lorsque les deux décharges de condensateur se suivaient, et l'appréciation comparative de l'intervalle des deux chocs était correcte, les deux chocs paraissant bien plus rapprochés pour un intervalle plus court des deux décharges.

Ainsi la sommation ne se traduit pas seulement par une efficacité plus grande de la deuxième décharge capable de franchir le seuil pour un voltage infraliminaire en cas de décharge unique, mais par un accroissement d'efficacité de la première décharge elle même, ce qui comporte un processus de *facilitation rétroactive*. Le phénomène s'est montré général chez tous les sujets pour des intervalles convenables.

Toutefois, chez un seul des sujets la perception du double choc mécanique persistait de façon constante jusqu'au seuil d'efficacité de la double décharge; chez les autres sujets, en général, au seuil de la double décharge, l'impression, qualitativement différente de celle du choc unique, ne comportait pas toutefois une perception distincte et nette des deux chocs mécaniques consécutifs. Mais, dès que le potentiel liminaire était accru de 1,5 volt, cette perception distincte se produisait toujours. Quand l'intervalle est seulement de 10 à 40 msec., il y a aussi une impression qualitativement différente de celle du choc unique, sans distinction nette de deux chocs, pour les voltages

intermédiaires entre le seuil du double choc et le seuil du choc unique. Nous allons donner quelques valeurs numériques chez trois sujets pour préciser le fait. Chez le sujet précédemment cité, voici des séries de mesures du voltage liminaire avec deux autres intervalles:

Nombre de chocs	1	2	1	2	1
Ecart de 83 msec.	124,5	108	127,5	112,5	127,5
——— 400 msec.	111	103,5	112,5	105	112,5

Dans tous ces cas, le sujet a perçu le double choc jusqu'au seuil.

Chez un autre sujet (chronaxie de 0,40 msec.) pour 83 msec. d'intervalle:

Nombre de chocs	2	1	2	2	1	2
Voltage liminaire	199,5	208,5	192	189	201	187,5

Le double choc est perçu déjà au début, à 199,5 v., et il l'est encore à 189 volts ensuite, le même voltage étant toujours inefficace avec une décharge unique.

Chez un troisième sujet, systématiquement, de nombreuses stimulations sont effectuées, avec décharge unique ou double, et la nature de la sensation de choc est indiquée chaque fois.

Avec 83 msec., d'intervalle (durée chronaxique d'excitation de 0,80 msec.), on obtient:

Nombre de chocs	1	2	1	2
Voltage liminaire	102	96	99	91

Avec 96 volts, puis avec 91 volts, déjà la sensation de double choc est accusée. Avec le même intervalle, le seuil avec décharge unique étant de 88 v., la double décharge donne une sensation à 80,5 v. Cette sensation n'est pas nettement de double choc, mais n'est pas non plus celle du choc unique, dès 82 v., le double choc est perçu nettement. Avec 166 msec. d'intervalle, le seuil pour la décharge unique est de 90 v., et pour la décharge double de 84 v.; à 85,5 v. la sensation de double choc est tout à fait nette; dans une autre série de mesures, le seuil pour la décharge unique est à 102 puis 103,5 v. A 97,5 v., avec double décharge, le double choc est perçu. Mêmes faits, chez ce sujet, avec des durées d'excitation, par décharge de condensateur, plus brèves (demi-chronaxie) ou plus longues (double chronaxie).

Voici donc le fait, d'allure éminemment paradoxale; une décharge inefficace, qui, si elle reste isolée, ne donne pas naissance à une sensation, devient efficace et provoque une sensation quand elle est suivie d'une autre décharge égale, et inégalement inefficace. Ce n'est pas seulement le première décharge qui, par un processus d'addition latente, rend efficace la seconde, mais c'est la seconde qui, par un processus de facilitation rétroactive, rend efficace la première.

IV. L'Accélération Réactionnelle Par Double Choc

La mesure des temps de réaction aux sensations de choc tactile provoquées par les décharges de condensateur de durée chronaxique indique une dé-

croissance très rapide de ces temps quand s'élève le voltage, à partir du seuil (marge réductible décroissant en fonction de la fonction quatrième de l'intensité de stimulation, en prenant pour unité d'intensité le voltage liminaire). Quand on stimule, par deux décharges consécutives de même intensité et de même durée, le temps de réaction est en général diminué; cette diminution est d'autant plus grande qu'on est plus près du seuil et que la marge réductible des temps est plus étendue. L'intervalle entre les deux décharges joue naturellement un rôle, l'action raccourcissante faisant défaut si l'intervalle est trop grand et faisant même place à une action allangeante près du seuil, mais se montrant maxima pour des intervalles d'une durée optima, sans que l'optimum ait été encore déterminé avec précision (l'optimum peut-être variable avec les sujets et aussi avec les niveaux d'intensité).

Pour comparer les temps de réaction avec un ou deux chocs électriques, on alternait la stimulation unique et la stimulation double. Voici, chez un sujet, entrainé et cohérent, des données relatives à ces valeurs des temps (en msec.), les intensités étant exprimées en multiples du voltage liminaire (avec choc unique) pris pour unité. Les deux valeurs indiquées à la suite représentent la moyenne arithmétique et le médian, qui est plus significatif, et la valeur entre parenthèses donne le nombre de mesures (Sujet P).

Intensité	Choc unique	Double choc à intervalle de				
		30 msec.	45 msec.	80 msec.	140 msec.	185 msec.
1	597–594(18)				475–472(18)	
1,5	491–476(19)				383–389(20)	
2	349–346(19)					358–365(19)
	325–329(15)	265–261(20)		293–303(15)		
	309–309(17)	292–292(17)				
3	271–272,5(18)		267–268(19)			

Voici d'autre part quelques déterminations faites sur divers autres sujets.

Sujet	Intensité	Choc unique	Double choc à intervalle de			
			13–14 msec.	24 msec.	30 msec.	40–45 msec.*
H	1	259–230(19)	242–236,5(20)			
H	1,05	185–183(13)	178–180,5(10)			
		200–206(13)				197–194(15)
S	1,25	308–294(14)		274–270(13)		
		310–319(8)	286–280(12)			299–310(8)
H	1,44	175–176,5(22)	176–177,5(22)			
B*	2	236–230(10)	223–222(7)		232–231(9)	
		364–360,5(10)				

* À 80 msec. le sujet B avec l'intensité 2 donne 285–278(11), et à 140 msec. il donne 312–295(9).

L'action raccourcissante augmente-t-elle par action de plusieurs décharges consécutives? Cela parait se dégager de quelques données, à condition que

l'intervalle entre les décharges consécutives ne soit pas trop long. Voici par exemple une série de mesures réalisées chez le sujet P avec des décharges séparées par des intervalles de 29 msec.

Intensité	Choc unique	Choc double	Choc triple	Choc quadruple
2	309–309 (9)	292–292 (17)	192–288 (16)	289–283 (17)

L'action devient moindre mais est encore sensible à la 4ème décharge (intervalle total de 87 msec.). Avec des séries continues de stimulations, l'action raccourcissante se montre en général plus grande qu'avec la double décharge. Chez le même sujet P, on obtient les valeurs suivantes des temps.

Intensité	Intervalle de 30 msec.		Intervalle de 80 msec.	
	Choc double	Chocs en série	Choc double	Chocs en série
2	265–261 (20)	282–280,5 (20)	293–303 (15)	281–287 (15)

Chez le sujet S voici les valeurs obtenues:

Intensité	Intervalle de 13 msec.		Intervalle de 40 msec.	
	Choc double	Chocs en série	Choc double	Chocs en série
1,25	286–280 (12)	246–242 (9)	299–310 (8)	264–246 (11)

L'action des décharges consécutives répétées peut donc être un peu plus grande que celle du double choc, le phénomène de sommation se traduit par l'accélération réactionnelle déclenchée dès le premier stimulus. Le fait du raccourcissement par les stimulations consécutives est en tout cas indéniable.

L'intervalle entre la première stimulation et la seconde, en cas de double décharge, peut être assez grand, mais à condition toutefois que les temps comportent encore une assez grande marge réductible. Au delà de 150–200 msec., on ne doit plus attendre d'action raccourcissante. Quand la marge réductible est épuisée, une réduction, du fait du double choc, ne peut naturellement plus être obtenue ou devient insignifiante (cas de l'intensité 3 chez le 1er sujet P, de l'intensité 1,44 chez le sujet H). Mais les données sont insuffisantes pour une analyse quantitative.

Le fait est que, de même que le seconde décharge peut augmenter rétroactivement l'efficience de la première, elle peut aussi raccourcir la latence de la sensation provoquée par cette première décharge. Comme la latence diminue lorsque croît l'intensité, il y a accord entre le fait de la facilitation et celui de la diminution de latence réactionnelle, qui témoigne d'une accélération du processus de l'éveil de la sensation. Tout se passe comme si, du fait de la décharge consécutive, l'efficience de la première décharge était augmentée de la même manière que par une élévation de son intensité objective.

V. Discussion et Essai d'Interpretation

L'efficacité d'une décharge brève de condensateur dont tous les faits d'enregistrement, sur l'animal, des potentiels d'action, permettent d'affirmer qu'elle engendre dans les fibres afférentes tactiles un influx unique, indique une possibilité d'éveil de la sensation n'impliquant pas un mécanisme itératif.

Lorsqu'à partir du seuil on augmente l'intensité de stimulation, à durée constante, ou la durée, à niveau constant d'intensité, on engendre une sensation de choc tactile plus intense, on met alors en jeu un nombre croissant de fibres et ce processus de recrutement progressif est à la base de l'accroissement d'intensité sensorielle; il y a d'ailleurs, lorsque le voltage augmente, une extension plus grande de la zone où se trouve localisée l'impression tactile, sur le territoire d'innervation de la branche sensitive excitée.

Quel que soit le mécanisme qui, dans l'excitation tactile physiologique, permet de différencier l'extension de l'excitation et son intensité, dans la stimulation électrique du nerf, les deux processus vont de pair. Mais, d'autre part la répétition de chocs successifs permet, à durée et niveau d'intensité constants de ces chocs, de provoquer une sensation plus intense (ou d'atteindre le seuil avec des stimuli isolément infraliminaires).

Dans la consécution de deux décharges, sous voltage égal, la seconde donne naissance à un choc tactile perçu plus intense. Cette sommation, indéniable, bien qu'elle n'ait pas été constatée par Schriever et Hegemann[2] est-elle de siège périphérique ou central? Gasser[3] a constaté, sur des nerfs vératrinisés ou préalablement soumis à une faradisation, que la répétition de stimulations électriques brèves pouvait entrainer des accroissements de potentiel témoignant d'un recrutement progressif de nouvelles fibres gagnées par l'excitation, et cela pendant une durée susceptible d'atteindre une demi seconde (gain au cours de l'application de 10 à 15 stimuli au rythme de 30 à la seconde). Mais, même si les nerfs tactiles, en place, soumis à des stimulations quasi-continues, pouvaient avoir des propriétés analogues à celles des nerfs préalablement faradisés, l'accroissement progressif d'intensité des chocs, perçus distincts (avec impression de type vibratoire), pourrait-il se confondre avec l'abaissement des seuils et le renforcement d'intensité constatés? Ce ne serait peut être pas impossible, s'il n'y avait cette facilitation rétroactive qui ne peut évidemment avoir son siège que dans les processus centraux.

Au niveau des centres, l'établissement progressif de l'état d'excitation préalablement au déclenchement d'une réponse répétitive des neurones synaptiques, observé par Barron et Matthews[4] dans la moelle, peut rendre compte d'un processus de sommation dans le temps, accéléré par action convergente de conducteurs afférents apportant simultanément les neuroquanta de leurs influx propres, ce qui permet de rendre compte d'une réduction de latence, alors même qu'il n'y aurait pas de réponse répétitive dans les fibres afférentes.[5]* La réduction, que nous avons observée, des temps de réaction, corrélative d'un recrutement progressif de fibres sensitives gagnées par l'excitation, pour les chocs isolés électriques (par décharge de condensateur de

* Pour des stimulations prolongées, la marge réductible, avec l'intensité, des temps de réaction, est essentiellement due à la réduction du temps d'action liminaire. Mais il existe une marge réductible pour les stimulations brèves, de l'ordre du dixième de seconde, interprétée par l'un de nous comme due à la réduction de l'intervalle d'un couple d'influx consécutifs quand la fréquence de la réponse s'élève avec l'intensité, le couple d'influx étant nécessaire pour le franchissement d'une synapse itérative.

durée chronaxique) quand croît l'intensité de ce choc (élévation de voltage) peut être ainsi élucidée. Mais la facilitation rétroactive n'est pas explicable par ce processus de l'établissement progressif de l'état d'excitation.

Nous avons été conduits à une hypothèse explicative qui a trouvé ultérieurement son appui expérimental dans les recherches de Lorente de No.[6] Sans avoir pris connaissance encore des études de ce dernier, une seule explication nous avait paru possible. La réponse de neurones synaptiques corticaux conditionnant l'éveil de la sensation tactile n'est pas encore engendrée aux environs du seuil quand ces neurones sont atteints par des influx suivant une voie d'accès directe, l'apport de neuroquanta étant insuffisant pour provoquer un niveau de l'état d'excitation correspondant au déclenchement de la réponse propre de ces neurones de type lent. Il faut que des influx, suivant une voie polysynaptique plus longue, viennent à leur tour converger sur les neurones en question, et compléter l'apport liminaire des neuroquanta nécessaires pour que la réponse se produise et que la sensation naisse—que le mécanisme de sommation réside en des modifications électriques cumulatives ou comporte un processus neurohumoral de libération progressive d'acétylcholine.

L'apport par voie directe—san doute nécessaire—est préparateur et facilitant, bien qu'inefficace. Si l'on est au dessous du seuil, même l'apport ultérieur, retardé, des voies polysynaptiques, est inefficace, la convergence ne fournissant qu'un nombre total encore insuffisant de neuroquanta. Mais si, entre l'arrivée des influx directs, et celle des influx retardés, survient une seconde volée d'influx directs, les influx retardés deviendront efficaces, complétant cette fois le niveau d'action liminaire par l'apport de leurs neuroquanta, et la sensation, qui n'était pas apparue avec le choc unique, sera déclenchée dans les mêmes conditions que si un accroissement d'intensité du stimulus avait permis, par action convergente d'un plus grand nombre de fibres, de rendre efficace l'apport retardé de neuroquanta par les voies polysynaptiques.

L'action, d'apparence rétroactive, s'explique en ce qu'elle s'insère pendant la phase de latence centrale au cours de laquelle s'élabore un état d'excitation par apport successif de neuroquanta suivant des voies polysynaptiques plus ou moins complexes, et réalisant l'itération répétitive qui n'existe pas dans les voies afférentes précentrales, précorticales même peut-on dire.

Les deux chocs successifs seront rendus efficaces, mais avec leur intervalle normal, car, pour la deuxième réponse, facilitée au niveau de neurones qui ne sont pas nécessairement les mêmes que ceux qui ont répondu au premier choc—par les apports préalables, elle ne se produira aussi que lorsque parviendront les influx retardés des voies polysynaptiques correspondant à la seconde volée d'influx afférents. On peut voir, sur la Fig. 2 ci-jointe, un schéma—évidemment très simplifié—de l'évolution de l'état d'excitation, en distinguant l'apport direct et l'apport retardé qui permet de rendre compte de la double réponse quand, à un niveau infraliminaire, la répétition du stimulus assure son efficacité. On y comprend également l'action accélératrice qu'exerce

le second choc, diminuant la latence réactionnelle à une même intensité de stimulation. En effet l'action facilitante exercée par l'apport suivant la voie directe qu'assure le second choc entraine, pour un même niveau d'intensité, un franchissement plus rapide du seuil de la réponse répétitive des neurones* lorsque surviennent les influx retardés des voies polysynaptiques.

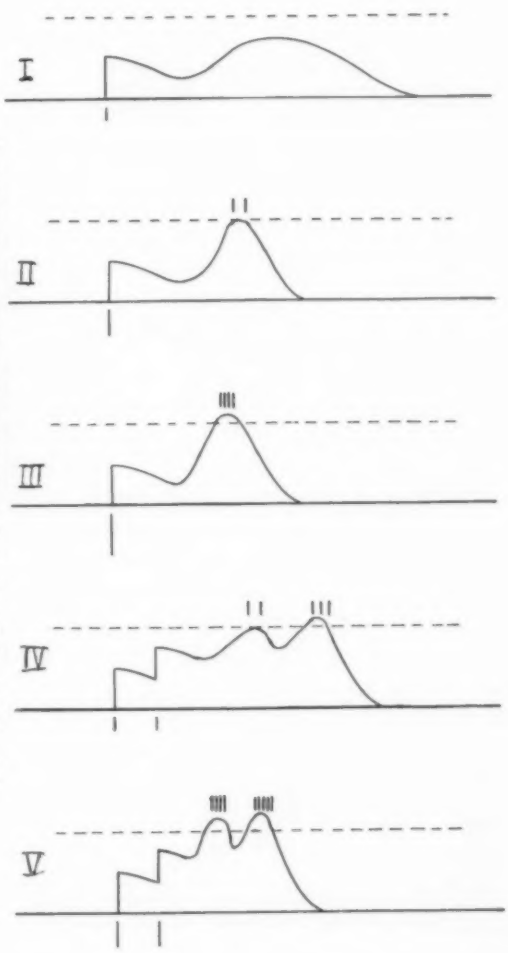

FIG. 2. Schéma de l'évolution de l'état d'excitation d'un esthésioneurone sous l'influence d'un choc électrique unique ou double porté sur une branche cutanée sensitive. Un influx direct infraliminaire est suivi d'une volée polysynaptique. Les traits placée en dessous indiquent les chocs électriques, dont l'intensité est marqué par la hauteur du trait. Les traits situés au dessus indiquent les influx déclenchés par l'esthésioneurone. En I, choc unique infraliminaire. En II choc juste liminaire, en III, choc supraliminaire. En IV double stimulation par chocs de même intensité qu'en I; l'insertion de l'influx direct du deuxième choc permet à la volée polysynaptique du premier choc d'atteindre le seuil d'excitation efficace; la deuxième volée polysynaptique survenant à son tour dépasse légèrement le seuil. En V, double stimulation par chocs de même intensité qu'en III. L'insertion de l'influx direct du 2° choc avant l'arrivée de la première volée polysynaptique accélère le franchissement du seuil d'excitation et accroit l'efficacité de la première réponse, la seconde atteignant un niveau un peu plus élevé que la première.

Le schéma se contente d'indiquer un apport retardé un peu massé, mais il est possible que les apports retardés se succèdent sur une période relativement longue, et qu'ainsi la réductibilité de latence puisse varier de façon continue dans une marge assez grande, marge réductible qui, déterminée par les mesures

* Avec un choc électrique unique donnant sur le nerf optique—homologue d'une voie médullaire sensitive—un seul potentiel d'action, on recueille, dans l'écorce striée, une réponse répétitive d'une certaine durée (réponse de 20 msec., accrue par la strychnine d'après les résultats de Bartley, O'Leary et Bishop).[7]

de temps de réaction se montre de l'ordre du dixième de seconde. D'autre part le fait que la sensation vibratoire peut être encore perçue à des fréquences assez élévées donne à penser que, parmi les esthésioneurones en connexion avec les fibres afférentes, un certain nombre répondent à chaque stimulus de choc, les autres étant en phase réfractaire, en sorte que le processus du double choc perçu puisse évoluer dans des neurones différents pour le premier et pour le second, l'arrivée des influx, suivant les voies polysynaptiques, qui aboutissent à plusieurs neurones, étant toujours nécessaire pour déclencher la réponse, aussi bien des neurones excités par le premier que de ceux excités par le second choc.

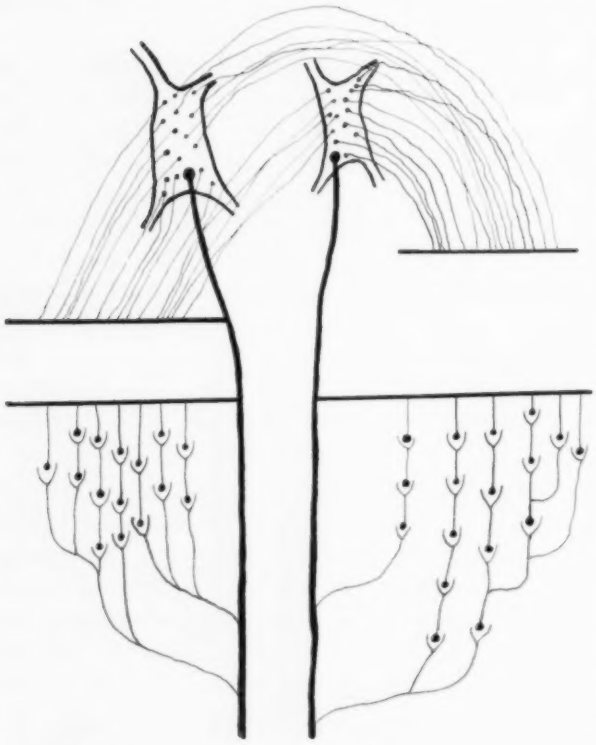

FIG. 3. Schéma relatif aux voies afférentes aboutissant à deux esthésioneurones corticaux, avec voie directe spécifiquement liée à un neurone défini, et voies dérivées polysynaptiques se rendant à l'un et l'autre neurone après un nombre variable de passages cellulaires entrainant des retards dans l'apport des influx (un grand nombre de synapses non indiquées correspondant à la coupure du schéma).

L'interprétation proposée s'accorde avec les faits étudiés par Lorente de Nó dans la stimulation des voies encéphaliques de la motricité oculaire du lapin, mettant en évidence l'arrivée retardée d'un bombardement d'influx par des voies polysynaptiques de neurones "internunciaux," de paradosioneurones Les chaines multiples de ces cellules interposées constituent, dans les centres cérébraux—et particulièrement dans l'écore—les véritables unités élémentaires de transmission, selon Lorente de Nó. Si les durées du délai dans l'excitation des noyaux oculomoteurs du lapin sont relativement brèves, ces durées, en ce qui concerne les polysynapses de l'homme peuvent être beaucoup plus longues.*

Au niveau de l'épanouissement principal des fibres afférentes sensitives en

* Des durées longues de facilitation s'observent dans les nerfs amyéliniques de Crustacés oú l'on peut noter, comme dans les centres, des variations lentes de potentiel caractéristiques de l'état d'excitation, étudiées par A. Arvanitaki,[8] qui a obtenu par exemple (effet pseudo-réflexe) une décharge répétitive afférente provoquée par sommation de 2 influx afférents isolément inefficaces, avec un intervalle de 0,24 sec.

d'innombrables ramifications, dans les couches moyennes du cortex, celles des grains, il existe des myriades de neurones, à interconnexions limitées à ce niveau (cellules en étoile), qui doivent intervenir dans ces relations polysynaptiques, tandis que d'autres cellules, moins nombreuses, du type pyramidal, assurent les connexions avec les régions supérieures du cortex et les transmissions conditionnant les processus perceptifs et l'intégration des excitations sensorielles dans le comportement psychologique.

Sans prétendre attribuer à des couches définies du cortex des fonctions absolument exclusives, attribution exclusive contre laquelle s'élève Lorente de Nó,[9] il paraît légitime, cependant, en l'état actuel de nos connaissances, d'attribuer, aux couches moyennes rôle important dans les processus de réception corticale, et les phénomènes sensoriels initiaux. Mais, après passage par les chaines polysynaptiques dont la réalité histologique est indéniable, l'éveil de la sensation, perçue avec retard, se fait-il dans les couches supérieures du cortex de projection, ou dans des régions avoisinantes c'est ce qu'il n'est pas possible d'affirmer à l'heure actuelle.

Conclusion

Le processus de facilitation rétroactive que nous avons mis en évidence avec un mode de stimulation relativement simple constitue en quelque sorte la contre partie de l'inhibition rétroactive qui, dans le domaine plus complexe des stimulations visuelles caractérise le métacontraste, découvert par Stigler, retrouvé par Fry, et systématiquement étudié par l'un de nous.[10,11,12]

Dans le métacontraste, il se produit, au niveau des centres ganglionnaires de la rétine, un raccourcissement de la réponse provoquée par une stimulation lumineuse locale quand survient ensuite—dans une certaine marge d'intervalles—une autre stimulation adjacente. Mais la sensation qui naît de la première excitation, raccourcie, peut être entièrement supprimée dans certaines conditions, et faire pleinement défaut. On peut penser que ce processus cortical d'inhibition est, lui aussi, rendu possible, grâce à cette phase de latence qui s'écoule entre l'arrivée des influx afférents directs et celle des influx différés suivant des voies longues polysynaptiques et dont le bombardement est nécessaire pour établir, dans les esthésioneurones, un niveau de l'état d'excitation (qui se traduit, d'après les données de Matthews, par une polarisation durable) suffisant pour déclencher la réponse conditionnant l'éveil de la sensation perçue.

D'autre part la marge réductible du temps de réaction qui, dans le cas de réponses afférentes répétitives, peut être ramenée à une réduction d'intervalle entre deux influx nécessaires pour le franchissement d'une synapse à caractère itératif,[13] devient explicable, même dans les cas où la première interprétation n'est plus possible,* en particulier quand, sans itération, se montre efficace pour éveiller une sensation le déclenchement d'un seul influx afférent, comme

* Des expériences sur les temps de réaction à des accroissements de brillance plus ou moins intenses, à partir de niveaux variables, se sont montrées incompatibles avec l'interprétation fondée sur la réduction de l'intervalle dans un couple d'influx.[14]

dans nos expériences de stimulation de fibres tactiles par un choc électrique bref.

C'est l'intervention des voies polysynaptiques de transmission cérébrale qui introduit une itération nécessaire, de durée réductible, lorsqu'un plus grand nombre de voies afférentes, se distribuant en un groupe d'esthésioneurones, sont simultanément mises en action par une stimulation plus intense. Ce bombardement, par apport des voies polysynaptiques, devient plus vite efficace, réalisant plus tôt le niveau de l'état d'excitation nécessaire pour que soit déclenchée la réponse conditionnant l'éveil de la sensation perçue, et que se produise le geste réactionnel que cette perception commande.

Le paradoxe de la rétroactivité fait place à la notion d'influences s'exerçant au cours de l'élaboration retardée de l'état d'excitation des esthésioneurones, en raison d'une participation nécessaire (sauf peut être dans des états d'hyperexcitabilité tels que ceux qu'engendre la strychninisation) des influx différés suivant les voies polysynaptiques corticales.

Résumé

Dans la stimulation par décharges brèves de condensateurs d'une branche sensitive cutanée (rameau digital du médian), chez l'homme, il a été constaté que, pour un niveau d'excitation infraliminaire, l'addition d'une seconde décharge consécutive, dans une assez grande marge des intervalles (dépassant le dixième de seconde) assurait la perception du choc tactile provoqué, non seulement par la deuxième, mais aussi par la première décharge, grâce à un processus de facilitation rétroactive. Cette facilitation s'est révélée encore par un raccourcissement des temps de réaction au choc tactile sous l'influence de l'intervention consécutive d'une seconde décharge, dans une marge analogue d'intervalles. L'interprétation de ce phénomène, d'apparence paradoxale, repose sur l'intervention d'un retard d'élaboration de la réponse des esthésioneurones conditionnant l'éveil de la sensation perçue par intervention nécessaire d'influx suivant des voies polysynaptiques—dont Lorente de Nó a établi l'existence par ses recherches histologiques et physiologiques—influx dont le bombardement débute un certain temps après l'arrivée d'influx directs inefficaces. A un niveau infraliminaire, le second choc, survenant entre l'influx direct et les volées retardées, peut rendre efficace le premier stimulus grâce à l'intervention de son influx direct, quand surviennent les influx qui déclenchés par le premier ont suivi les voies polysynaptiques; et, à un niveau supraliminaire il accélère l'établissement d'un niveau efficace et diminue ainsi la latence.

REFERENCES

1. Piéron, H., et Segal, J. La sensibilité tactile digitale étudiée par stimulation électrique du nerf cutané. *C. R. Soc. Biol., Paris*, 1938, *128:* 762.
2. Schriever, et Hegemann. Untersuchungen über die elektrische Erregbarkheit. IV. Über Summation. *Z. Biol.*, 1933, *94:* 253–363.
3. Gasser, H. S. Recruitment of nerve fibers. *Amer. J. Physiol.*, 1938, *121:* 193–202.
4. Barron, D. H., et Mathews, B. H. The interpretation of potential changes in the spinal cord. *J. Physiol.*, 1938, *22:* 276–321.

5. PIÉRON, H. Recherches sur les lois de variation des temps de latence sensorielle. *Ann. Psychol.*, 1914, *20:* 17–96. Recherches expérimentales sur la marge de variation du temps de latence de la sensation lumineuse. *Ibid.*, 1926, *26:* 1–30. L'interprétation des retards réductibles de latence sensorielle. *C. R. Soc. Biol., Paris*, 1932, *111:* 587–588. L'analyse des temps de réaction. *Ann. Psychol.*, 1933, *33:* 106–117.
6. LORENTE DE NÓ, R. Synaptic stimulation of motoneurons as a local process. Analysis of the activity of the chains of internuncial neurons. *J. Neurophysiol.*, 1938, *1:* 195–206; 207–244.
7. BARTLEY, S. H., O'LEARY, J., and BISHOP, G. H. Modification by strychnine of response of the optic cortex. *Proc. Soc. exp. Biol., N. Y.*, 1937, *36:* 248–250.
8. ARVANITAKI, A. *Les variations graduées de la polarisation des systèmes excitables.* 1938. (vide p. 101–106 et fig. 50).
9. LORENTE DE NÓ, R. Architectonics and structure of the cerebral cortex. In FULTON, *Physiology of the nervous system*, Oxford University Press, 1938 (p. 291–330).
10. STIGLER, R. Chronophotische Studien über den UmgebungsKontrast. *Pflüg. Arch. ges. Physiol.*, 1910, *134:* 365–475.
11. FRY, G. A. Depression of the activity aroused by a flash of light by applying a second flash immediately afterwards to adjacent areas of the retina. *Amer. J. Physiol.*, 1934, *108:* 701–707.
12. PIÉRON, H. Le processus du métacontraste. *J. Psychol.*, 1935, *31:* 5–24.
13. PIÉRON, H. *La connaissance sensorielle et les problèmes de la vision.* Paris, 1936. (vide p. 29–30).
14. DURUP, G., et PIÉRON, H. Les temps de réaction à des accraissements brefs de brillance. *Ann. Psychol.*, 1938, *38:* 148–161.

ABLATIONS OF FRONTAL CORTEX IN CATS WITH SPECIAL REFERENCE TO ENHANCEMENT OF THE SCRATCH REFLEX

F. KEITH BRADFORD

From the Division of Neurology and Neurosurgery, University of Chicago

(Received for publication January 30, 1939)

ALTHOUGH numerous investigators have studied cats following extirpation of various parts of the cerebral cortex, especially the area about the cruciate sulcus, their accounts make no reference to certain reflexes and modifications of behavior herein described. Emphasis will, therefore, be placed upon these phenomena, and findings corroborating previous investigators will only be mentioned as they relate to these data.

METHODS

Pentobarbital sodium, 25 to 35 mg. per kg. intraperitoneally, was the only anesthetic used. All operations were conducted under aseptic conditions. A spatula was used for the subpial dissection. The frontal sinuses were opened widely on one or both sides except in the operation on Cat 118. The frontonasal ducts were occluded with muscle before closing. Only one operation was performed on each cat. It was found most convenient to use a horsehoe shaped incision with the base toward the forehead. The cats were sacrificed by administering pentobarbital sodium, 50 mg. per kg. intraperitoneally, and opening the chest in order to perfuse the brain *in situ* with physiological saline followed by 10 per cent formalin. After further fixation in formalin, dehydration, and embedding in nitrocellulose, serial sections were cut 40 μ thick. Every 30th section was stained by Weil's[13] technic for myelin.

RESULTS

Bilateral Preparations

In 4 cats (Nos. 119, 121, 124, and 125) the frontal cortex on both sides was extirpated, including in each instance the sigmoid gyri, most of the gyrus proreus, and part of the area surrounding the sigmoid gyri. Since the postoperative behavior of all 4 cats was similar, they will be described first as a group. In none was it possible to elicit the 4 placing reactions of Bard[1] during the survival period. The hopping reactions were markedly impaired. For 1 or 2 days it was necessary to feed these cats by spoon, but soon they ate spontaneously. After a week of untidiness they groomed and soon could not be distinguished from normal cats by their coats. None of the animals showed "sham rage," but at times during the first postoperative month all except Cat 121 showed momentary spitting and fighting, poorly directed and lasting but a few seconds. All 4 cats were in almost constant motion, their tails in particular being abnormally active. The cutaneous maximus muscle frequently twitched, especially when the vertebral column was tapped.

Cats 121 and 124 showed postoperatively for 2 months almost constant purring which then became less frequent. Mistreatment tended to increase

the purring which, in the latter months of survival, occurred only after handling, usually of an unpleasant sort. Strangely, purring was never observed in Cats 119 and 125. These 4 cats tended to watch an object rubbed across the wire of the cage as long as it was kept in motion. When they were allowed to run loose, they almost constantly followed a moving person, but if he stopped interest appeared to be lost. The response to petting was diminished. They were easily handled, but became restive upon being held. *Gait* was severely disturbed for the first few days. It was usual to see one of these cats fall after shaking. Another temporary disturbance was the placing of a forefoot on the dorsal rather than on the plantar surface. From the time of operation on, all 4 cats showed increased extensor tonus in all extremities. The tonic neck reflexes of Magnus[8] were found transiently in but one cat (No. 119). During the entire survival period these cats kept their claws out more than normally, frequently getting them hooked in the wire cage. On being held in the supine position, the body and neck were flexed forward and then the forelegs with claws extended clutched at the abducted hind legs, pulling the shoulders through. The hind legs were next brought into a standing position, and the animal walked off.

Scratch reflex. Cats 121, 124, and 125 showed a remarkable accentuation of the scratch reflex. Cat 119 was not examined for the scratch reflex since death occurred before the increase in the reflex was observed in Cat 121. In cats the scratch reflex is elicited in the same manner as the auriculogenital reflex.[3] Tweaking the cartilaginous portion of the external ear between the forefinger and thumb from behind, or rapidly rotating the index finger or a cotton swab placed in the external acoustic meatus was the most satisfactory method of eliciting it. Stimulation of parts of the head and neck other than the external ear, or stimulation of the chest and flank never produced the scratch reflex in either normal or operated cats. Faradic stimulation produced a response only when applied to the skin of the external acoustic meatus.

Cat 121 showed the most remarkable increase in the scratch reflex which became apparent 2 weeks after operation and persisted until the animal was sacrificed 3 months later (Fig. 1). Spontaneous scratching resulted in ulceration of the skin over the occiput and back of the neck. In Cat 125 the scratch reflex became hyperactive on the tenth postoperative day, and in Cat 124 only after 6 postoperative weeks. The hyperactivity of the scratch reflex was out of all proportion to that in normal cats. Irrespective of the cat's position, stimulation of one ear would cause flexion of the trunk and neck to that side with effective and continued scratching by the homolateral hind leg. With the cat held in the erect position by the head and one ear stimulated, the homolateral hind leg was lifted from the floor, undergoing rhythmic scratching movements which in this case were ineffective. If both external ears were stimulated simultaneously, there were clonic contractions of both hind legs joined later by the forelegs. Then the head drew back simulating a clonic convulsion which lasted only during the period of stimu-

lation. This caused marked restlessness and miaowing. In normal cats such maneuvers as the last caused only a display of anger, and stimulation of one ear elicited the scratch reflex only when the position in which a cat was lying was convenient for scratching. Even so, the scratching was frequently abortive, contrasting strikingly with the sustained compulsory scratching of the operated cats which would struggle awkwardly from side to side, scratching alternately with the hind legs as the ears were alternately stimulated.

Auriculo-genital reflex. When the external ear was stimulated in one of

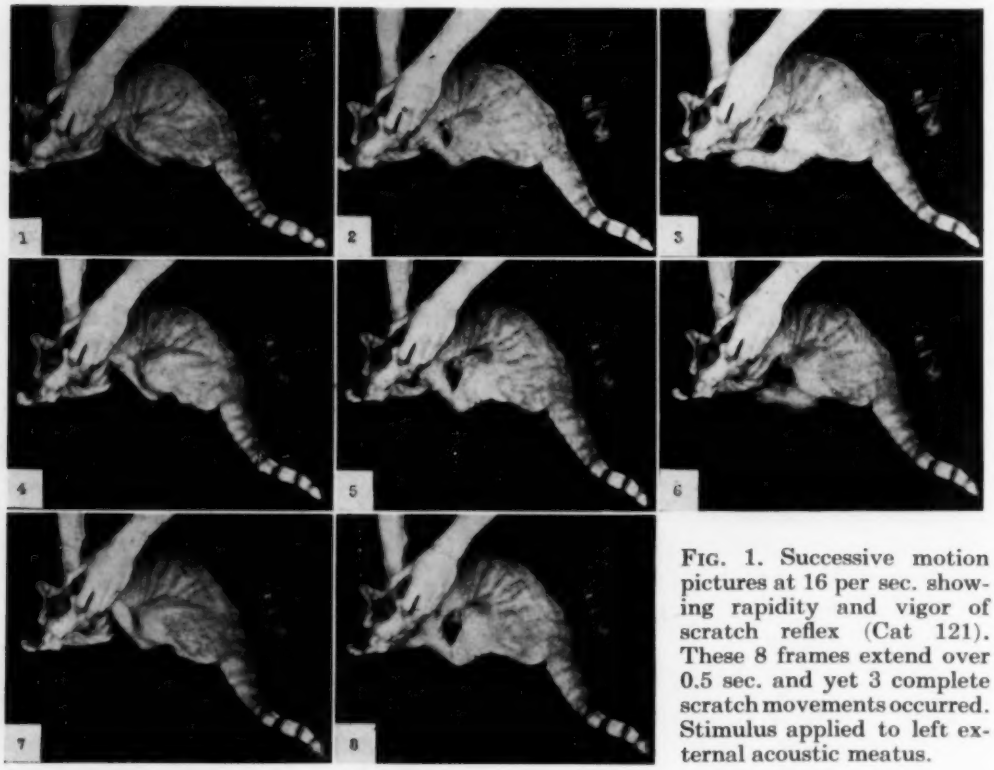

FIG. 1. Successive motion pictures at 16 per sec. showing rapidity and vigor of scratch reflex (Cat 121). These 8 frames extend over 0.5 sec. and yet 3 complete scratch movements occurred. Stimulus applied to left external acoustic meatus.

the ways just described to elicit the scratch reflex, there also resulted contraction of the subcutaneous muscle about the penis or vagina.[3] This response, present in normal cats, could be elicited far more easily in Cats 121, 124, and 125 than in normal animals, although there was great variability in the ease of elicitation in the normals. Brushing the hand across the ear in a manner to fold it forward and downward frequently elicited the reflex in the operated animals although this was an inadequate stimulus in normal cats.

"Going-under-or-over-fence" reaction. In Cat 121, and to a lesser degree in Cats 124, and 125, a reversal of the usual reaction to gentle stroking of the back was observed. Cat 119 was not studied for this response because

it was not observed until after this cat's demise. A normal cat almost invariably arches its back when gently stroked. But these cats did just the opposite, making the back concave beneath the stroking fingers. This response was obtained on the 12th postoperative day, continuing throughout the survival period in Cat 121, although during the last month it was obtained only when the cat was in motion. As the cat moved beneath the gently stroking finger the back was lowered markedly, and as the sacrum came under the finger the pelvis was lowered almost to the floor and the hind legs clambered awkwardly behind the animal in a manner identical to that of a cat crawling through a hole under a fence (Fig. 2). If the undersur-

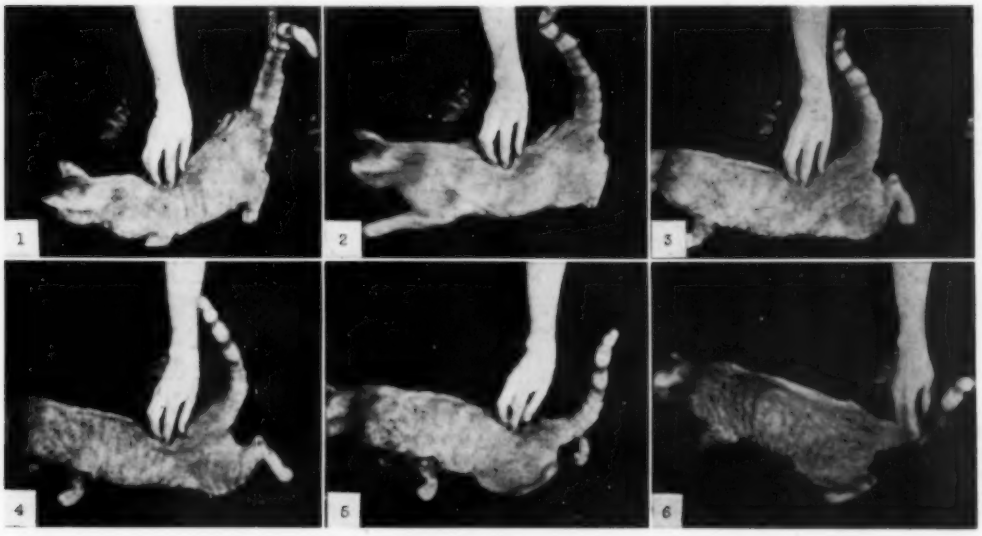

FIG. 2. Six frames from a motion picture have been selected to demonstrate the "under fence" reaction in Cat 121. They are reproduced in order, representing a 2 second period. The fingers can be seen touching the back lightly, and yet the response is as if the cat were trying to pass under a fence.

face of the abdomen was gently stimulated with the finger the back was arched greatly, and if the cat was in progress, the hind legs were raised awkwardly as if to clamber over a board when this point was reached.

"*Climbing discharge.*" With the exception of No. 121, these 4 cats exhibited an unusual type of motor discharge during the first few postoperative days lasting up to 2 weeks. When these cats were held upright and fed with a spoon, they settled back in a characteristic position on their haunches and for several mouthfuls would swallow well enough. But often upon continuing this, they became restless, the pupils dilated, and jumping movements occurred. If this discharge was encouraged by jumping the animal up and down holding it by the chin and scruff of the neck, the springing gained in extent and was accompanied by increasingly violent climbing movements of the forelegs. If, at the height of the discharge, the cat was

held with feet toward the side of a wire cage, it rapidly but awkwardly climbed up. To keep it from falling backward it was necessary to retain a grip on the scruff of the neck, for the climbing movements were not sufficiently accurate to hold constantly to the wire cage. Cat 124 voided once at the termination of such a discharge. At no other time during the survival periods did any of these 4 cats attempt to climb the wire cage, nor, after 2 weeks postoperative, could such a reaction be produced. The "climbing discharge" appeared identical to that observed in several unanesthetized cats when bipolar electrodes implanted in the hypothalamus were stimulated with faradic current.

Groping and grasping. For the first postoperative week Cat 125 showed definite groping and grasping in the forelegs when held in an upright position on its haunches. One forepaw would make rhythmic groping movements. If it came in contact with something, it would be brought strongly down toward the cat's side. Then the other forepaw would similarly grope and only be brought toward the body if it met an object in its groping. Although the groping and grasping were constant from the 2nd to the 7th postoperative day, many subsequent attempts to elicit this reaction failed.

Licking and biting response. Cat 124 showed a peculiar reflex elicited by scratching over the sacrum just anterior to the base of the tail. Whenever stimulation was made in this manner, the cat would begin to lick the air, the floor, or even lick and bite his own forelegs. Bard and Rioch[2] have described such a reflex in decorticate animals, which was useful in getting them to eat. But in their decorticate cats the reflex was obtained from stimulation anywhere on the cat's body. The small area over the sacrum was the only area from which the reflex could be elicited in this cat and, after it was discovered about 3 weeks postoperative, the licking and lapping response never failed to appear upon stimulation here. Olmsted and Logan[10] mention a reflex occurring in a female cat with destruction of rostral cortex on both sides which was elicited from the same area as was the "licking response." This consisted of elevation of the tail and flexion of the hind legs into a squatting position. This was interpreted as a sexual reflex.

With the exception of Cat 119, these 4 cats lived until sacrificed. Cat 119 ate well and kept its coat neat and clean until the 33rd postoperative day when it was observed circling wildly around the large cage it occupied with several other cats. The pupils were maximally dilated, giving a wild, frightened appearance. When Cat 119 was separated from the other cats, the violent overactivity continued. Even *in extremis* there were occasional violent outbursts of activity. The cat expired the following day. Postmortem examination disclosed only the expected ablation without evidence of any operative complication. Cats 121, 124, and 125 were allowed to survive 93, 162, and 161 days respectively.

Extent of ablations. In Cat 119 destruction on both sides included rostrally the anterior and posterior sigmoid gyri and the third of the gyrus proreus proximal to the anterior sigmoid gyrus (Fig. 3). Posteriorly and

laterally there was destruction of the coronal gyrus, the anterior suprasylvian gyrus, and the anterior part of the gyrus lateralis on the right and to a slightly lesser extent on the left. Descending degeneration could not be followed with a myelin sheath stain because of the relatively short survival period (34 days).

The ablation in Cat 121 was like that of Cat 119 except that on the left the gyrus proreus was removed but for a small ventral fragment, and there was slight damage to the rostral tips of the caudate nuclei. Coronal sections stained for myelin showed on each side a compact degenerated bundle which could be followed from beside the head of the caudate nucleus into the medial half of the posterior limb of the internal capsule. The degenerated

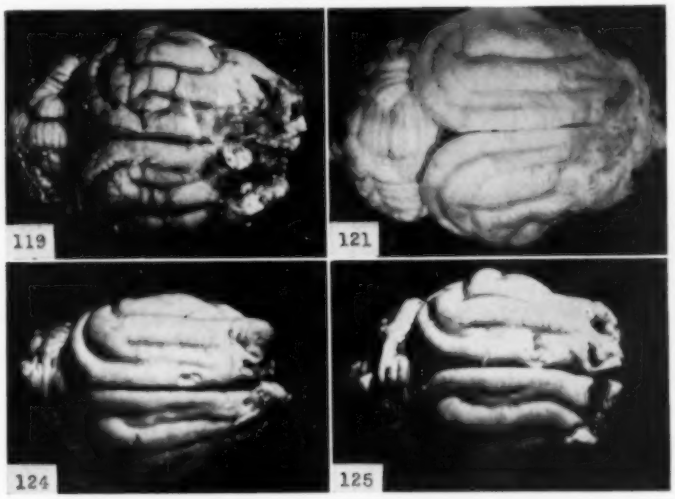

FIG. 3. Dorsal view of the brains of Cats 119, 121, 124, and 125 showing in each the bilateral ablation of rostral cortex.

fibers were rearranged in the cerebral peduncle to form a crescent next to the substantia nigra. In the pons the degenerated bundles were situated laterally and toward the tegmentum. The pyramids of the bulb were completely degenerated and severely atrophied.

In Cat 124 the ablation included bilaterally most of the gyrus proreus while in Cat 125 only one third of each gyrus proreus was included. The myelin degeneration in both resembled closely that occurring in Cat 121.

Unilateral preparations

Three cats with operations limited to the right side (117, 118, and 120) are included in this report chiefly to corroborate the observations of previous investigators. Cats 117 and 118 behaved so similarly that they can be described together. There was permanent increase in the extensor tonus of both left extremities as demonstrated by supporting the animal by head

and tail or by placing it in the supine position with the neck extended. From the first postoperative day throughout survival the placing reactions were absent in the contralateral (left) extremities. There was attitudinal abnormality of the affected extremities and failure to use them properly in leaping from tables, etc. Both cats showed a response to petting on the right side only. The scratch reflex could not be elictied from the left ear (side opposite the ablation) for the first few weeks postoperative although easily elicited from the right ear. However, after 2 months the reflex was as great or sometimes greater when elicited from the contralateral (left) ear. In addition, Cat 118 showed the "climbing discharge" as described for the bilaterally operated cats for several days during the second postoperative week. The "fear reaction" at the hissing sound of escaping air was also present. In retreating from this sound, Cat 118 once wedged its head firmly beneath a refrigerator.

Cat 120 had a very small cerebral ablation limited to the sigmoid gyri on the right side. The contralateral foreleg showed complete absence of the placing reactions, but the hind leg was not entirely deficient although it contrasted markedly with the homolateral hind leg. The left foreleg showed more constant attitudinal abnormality than the left hind leg. Personality and response to petting were unchanged. The scratch reflex elicited from the homolateral (right) ear was active, from the contralateral (left) ear at first absent, until they became equal about 2 months postoperative. Cats 117, 118, and 120 were allowed to survive 245, 174, and 633 days respectively.

Extent of ablations. In Cat 117 destruction limited to the right side included the anterior and posterior sigmoid gyri, the adjacent half of the gyrus proreus, the coronal gyrus, the anterior suprasylvian gyrus, and the anterior part of the lateral gyrus. Coronal sections stained for myelin showed degeneration limited to the right side similar to that described for the bilaterally operated animals. In Cat 118 the ablation was similar to that in Cat 117, but (probably as a result of pressure on the anterior part of the hemisphere to bring about hemostasis) cystic degeneration of the hemisphere occurred, leaving intact only a small portion of the temporal and occipital cortex. Sections stained for myelin revealed complete degeneration of the internal capsule, cerebral peduncle and pyramid on the affected side. The small ablation in Cat 120 was limited to the anterior and posterior sigmoid gyri on the right but did not include all the cortex buried in the cruciate sulcus. The degeneration was less marked than in the other cats. The right pyramid was incompletely degenerated, but atrophied to about half the size of the left.

Discussion

The scratch reflex in the cat can be readily elicited only from the region of the external ear, the same area from which the afferent end of the reflex arc for the auriculo-genital reflex takes origin. These 2 reflexes differ widely in their activity in normal cats. Since the auriculo-genital reflex is frequently

very active in normal cats, it is difficult to judge finally in regard to its exaggeration. On the other hand, the scratch reflex, although variable, is partially inhibited in normal cats, making accentuation clear when it does occur.

Cats 117, 118, and 120 showed a temporary absence of the scratch reflex when attempt was made to elicit it from the ear opposite the ablation, although it could be elicited from the homolateral ear. This may have been merely a coincidence since the response to stimulating the ears later became equal. It is mentioned because the bilaterally operated cats (121, 124, and 125) underwent a period of 10 days or longer when the scratch reflex could not be obtained after operation. It is rather to be suspected that one frontal pole will maintain an inhibitory activity on underlying centers having to do with activity of the extremities on both sides. Fulton[4] and his coworkers have shown in monkeys that area 4 or 6 preserved on one side alone influences the tonus and reflex activity of the homolateral as well as the contralateral extremities.

Bard and Rioch[2] report that rubbing the side of the head of a decorticate cat caused, at times, turning of the head to that side followed by attempts to scratch with the ipsilateral hind foot. If the ear had been stimulated rather than merely the side of the head, exaggeration of the scratch reflex would probably have been observed in their decorticate cats similar to that observed here in cats with ablated frontal poles. Olmsted and Logan,[10] King,[6] Langworthy,[7] and Magoun and Ranson[9] have reported the motor findings in cats with similar bilateral ablations of rostral cortex, but no reference is made to the scratch reflex.

The "climbing discharge" evidently represents a discharge of lower centers, probably hypothalamic. The reaction is certainly a purposive one, although disorderly. It was present only in the immediate postoperative period. This reaction corresponds closely to that reported by Rioch and Brenner[11] from stimulation of the ventricular floor at and in front of the anterior commissure in cats 10 days or longer following decortication. In their cats 5 to 10 seconds of faradic stimulation was followed by a sudden burst of activity in the form of violent springing and running movements continuing for one minute after stimulation had ceased. Two explanations of the "climbing discharge" seem possible. First, the fibers degenerating as a result of the ablation may have influenced diencephalic centers in a way to make them more irritable for a period not greater than 2 weeks. Second, other inhibitory mechanisms, cortical or subcortical, may have replaced the ablated area in its inhibitory activity at the end of 2 weeks. The transient groping and grasping observed in Cat 125 must likewise have been due to transient overactivity of lower centers, probably hypothalamic.

The "going-under-or-over-fence" reaction represents the uncontrolled activity of a useful mechanism. The movements resemble closely those of a normal cat going through a hole under a fence or clambering over a board. But the gentle stroking of the back with one finger in an anteroposterior

direction necessary to elicit the "under-fence" reaction in the bilaterally operated cats caused arching of the back in normal cats. Since these reactions diminished in the ease with which they were elicited during the last weeks of survival, it seems probable that some other inhibitory mechanism gradually replaced the ablated rostral cortex. Bard and Rioch[2] described behavior in one cat after bilateral removal of neocortex which somewhat resembles the "under-fence" reaction, but may be related to sexual activity. When its back was rubbed or scratched this cat relaxed, abducted the hind legs, depressed its tail, and dragged itself forward with the forelegs, growling loudly.

A stereotyped licking response was noted by Schaltenbrand and Cobb[12] and substantiated by Bard and Rioch[2] in decorticate cats. The reflexogenous zone included the neck, shoulders, back, and genital regions. It is interesting that this same response was present in Cat 124 but not in the other 3 bilateral frontal pole ablations, and in Cat 124 could be elicited only over the dorsum of the sacrum near the base of the tail. However, when elicited here, the reflex was fully developed.

Purring in response to petting or fondling is reported in decorticate cats by Schaltenbrand and Cobb[12] and by Rioch and Brenner.[11] In a series of 4 decorticate cats Bard and Rioch[2] report that purring was observed in only one cat, and then on only one occasion. Gibbs and Gibbs[5] report purring as a result of electrical stimulation in the infundibular region in 3 of 400 cats stimulated. Purring, however, in Cats 121 and 124 was almost constant during handling for the first 2 months postoperative after which it was less frequently observed. Rough handling or the deliberate pinching or roughing of these cats increased rather than decreased the intensity of the purring. Cats 119 and 125 with similar ablations, but with less destruction of the gyrus proreus on each side, were never observed to purr. It is possible that the ablation of both frontal poles released other undisturbed cortical areas from inhibition, or that diencephalic centers were similarly released. In the latter case the absence of purring in Bard's decorticate cats is not explained.

Summary

1. Ablation of frontal cortex around the cruciate sulcus in cats produced in the bilateral experiments the behavior described by previous investigators including the absence of the placing reactions. In the unilateral experiments the behavior was unchanged, but the placing reactions were destroyed in the contralateral extremities.

2. The "climbing discharge," groping and grasping, the licking and biting response, exaggeration of purring, and the "under-or-over-fence" reaction were correlated with the observations of previous investigators.

3. Marked enhancement of the scratch reflex which occurred 2 to 6 weeks after bilateral frontal ablations persisted throughout survival periods up to 162 days.

4. Unilateral ablation of frontal cortex effected no enhancement of the scratch reflex, but only transient abolition in the contralateral extremities.

REFERENCES

1. BARD, P. Studies on the cerebral cortex. 1. Localized control of placing and hopping reactions in the cat and their normal management by small cortical remnants. *Arch. Neurol. Psychiat., Chicago*, 1933, *30:* 40–74.
2. BARD, P., and RIOCH, D. MCK. A study of four cats deprived of neocortex and additional portions of the forebrain. *Johns Hopk. Hosp. Bull.*, 1937, *60:* 73–147.
3. BRADFORD, F. K. The auriculo-genital reflex in cats. *Quart. J. exp. Physiol.*, 1938, *27:* 271–279.
4. FULTON, J. F., and KENNARD, MARGARET A. A study of the flaccid and spastic paralyses produced by lesions of the cerebral cortex in primates. *Res. Publ. Ass. nerv. ment. Dis.*, 1932, *13:* 158–210.
5. GIBBS, E. L., and GIBBS, F. A. A purring center in the cat's brain. *J. comp. Neurol.*, 1936, *64:* 209–211.
6. KING, W. T. Observations on the rôle of the cerebral cortex in the control of the postural reflex. *Amer. J. Physiol.*, 1927, *80:* 311–326.
7. LANGWORTHY, O. R. The area frontalis of the cerebral cortex of the cat, Its minute structure and physiological evidence of its control of the postural reflex. *Johns Hopk. Hosp. Bull.*, 1928. *42:* 20–65.
8. MAGNUS, R. Körperstellung und Labyrinthreflexe beim Affen. *Pflüg. Arch. ges. Physiol.*, 1922, *193:* 396–448.
9. MAGOUN, H. W., and RANSON, S. W. The behavior of cats following bilateral removal of the rostral portion of the cerebral hemispheres. *J. Neurophysiol.*, 1938, *1:* 39–44.
10. OLMSTED, J. M. D., and LOGAN, H. P. Lesions in the cerebral cortex and extensor rigidity in cats. *Amer. J. Physiol.*, 1925, *72:* 570–582.
11. RIOCH, D. MCK., and BRENNER, C. Experiments on corpus striatum and rhinencephalon. *J. comp. Neurol.*, 1938, *68:* 491–507.
12. SCHALTENBRAND, G., and COBB, S. Clinical and anatomical studies on two cats without neocortex. *Brain*, 1931, *53:* 449–488.
13. WEIL, A. A rapid method for staining myelin sheaths. *Arch. Neurol. Psychiat., Chicago*, 1928, *20:* 392–393.

TEMPERATURE REGULATION IN CATS WITH THALAMIC LESIONS*

GEORGE CLARK, H. W. MAGOUN, AND S. W. RANSON
From the Institute of Neurology, Northwestern University Medical School, Chicago, Illinois

(Received for publication January 19, 1939)

IT IS now generally agreed that the hypothalamus plays an important part in temperature regulation (Ranson and Magoun, 1939). The remainder of the diencephalon does not appear to participate in this function, but it has seemed desirable to secure additional information on this point.

METHODS

With the aid of the Horsley-Clarke instrument, moderate sized lesions were placed bilaterally in various parts of the thalamus in 9 cats. In 6 other cats large lesions were made and in 3 of these in order to secure the maximum destruction without killing the animals, the operation was performed in two stages, first on one side and then the other side of the thalamus, with a period of 8 to 16 days intervening. A needle-like bipolar electrode with the bare tips of the constituent wires separated by 2 mm. along the long axis of the needle was used and through it a direct current of 3 mA. was passed for 1 minute to produce a lesion. In the 3 cats in which the greatest injury was inflicted 9 punctures were made on each side and 3 lesions were placed along each of the 3 lateral punctures and 2 along each of the other 6. The 21 lesions all fused together to form one very large lesion which after the second operation was united with a similar one on the opposite side.

Daily records were made of the rectal and environmental temperature and at varying times after the operation tests were made to determine the ability of the animals to withstand heat and cold. These hot and cold box tests were similar to those described by Teague and Ranson (1936) except that in the hot box a fan was provided to keep the air in circulation. The temperature of the hot box was 104°F. and that of the cold box varied considerably but averaged around 40°F. Before they were sacrificed each of the 6 cats with large lesions were decorticated under ether and as they recovered from the anesthetic they were watched for decorticate panting. They were then killed by bleeding and the brains perfused with 10 per cent formalin. Serial sections were cut through the diencephalon and alternate sections were stained by Weil's method for myelin sheaths and cresyl violet for cells.

RESULTS

The 9 cats with moderate sized lesions may be considered together as group A and the 6 with large lesions as group B. In both groups the rectal temperatures were above the normal average on the first postoperative morning. In group A the temperatures were around or slightly above the upper limits of normal. In group B the 3 cats (13, 14, 15) with the largest lesions had temperatures ranging from 104.4 to 105.1°F. on the first morning following each of the 2 operations. In no case was a subnormal temperature encountered. By the third day the cats began to eat voluntarily. The 3 cats in which the damage was at first unilateral circled to the side opposite the lesions for at least 3 days following the first operation. In none of the cats was there any indication of catalepsy or somnolence.

* Aided by a grant from the Rockefeller Foundation.

The results of the hot and cold box tests are given in Table 1. At the head of the table are the average results obtained from 94 tests performed on normal cats. While the average panting level, or rectal temperature at which panting began was 103.2°F., variations between 105.4 and 101.4°F. were encountered in normal cats. The table shows that all the cats of both groups panted in response to heat and that although the panting level was in most instances higher than the average for normal cats it was in each case

Table 1

Cat no.	Hot Box Tests				Cold Box Tests				Decortications	
	Days P.O.	Panting level	Rise above initial temp.	Final resp. rate	Days P.O.	Rectal temp. at start of test (F.)	Rectal temp. at end of test (F.)	Change	Highest resp. rate	Panting
Normal averages		103.2	1.6	214		101.2	101.0	−0.2		
Group A										
1	6	104.1	1.4	160	9	101.9	100.4	−1.5		
2	6	103.8	1.8	210	9	103.1	101.9	−1.2		
3	15	103.6	3.4	150	16	100.6	99.8	−0.8		
4	31	103.9	2.0	130	30	101.9	100.2	−1.7		
5	19	103.6	2.2	300	18	101.2	101.4	+0.2		
6	53	104.2	2.7	180	53	102.1	100.2	−1.9		
7	44	105.1	3.9	130	60	101.2	100.4	−0.8		
8	49	103.8	2.2	190	49	101.4	101.1	−0.3		
9	59	103.0	1.8	180	58	101.6	100.0	−1.6		
Group B										
10	13	103.1	2.0	160	14	102.3	100.4	−1.9	44	no
11	18	104.2	1.6	210	21	102.2	100.1	−2.1	166	yes
12	13	103.2	1.0	180	16	101.9	101.0	−0.9	156	yes
13	27	103.1	1.1	160					120	yes
14	48	103.5	1.1	150	17	102.3	102.0	−0.3	120	yes*
15	27	103.4	0.1	240					180	yes

* Required facilitation afforded by opening mouth.

within the range of normal variation. The tests in the hot box, therefore, revealed no significant disturbance in temperature regulation. All of the cats reacted normally in the cold box and after 3 hours exposure to a temperature around 40°F. only one cat had a temperature as low as 99.8°F. These tests in the hot and cold box were as a rule made 2 weeks or more after the placing of the lesions, the exact number of days being indicated in the table.

As a final test the 6 cats of group B were decorticated under ether anesthesia 28 to 53 days after the last operation. During recovery from the anesthesia decorticate polypneic panting occurred in all but one (Cat 10). Another (Cat 14) panted only when the mouth was forced open. Stretching

the muscles of mastication apparently acts as a stimulus favoring panting (Kleyntjens, 1937). The failure of Cat 10 to show decorticate panting, although it did pant in response to heat, cannot be attributed to the lesion, for the area destroyed in this cat was also destroyed in Cats 13, 14 and 15 which did pant following decortication.

The small lesions in the cats of group A were placed at various positions in the thalamus damaging chiefly the medial nuclei but also involving some of the nuclei of the lateral group. In the first 3 cats of group B the lesions were intermediate in size between those in the last 3 of this group and those in the cats of group A. In Cats 10 and 12 the damage extended forward from the rostral border of the habenular nuclei. In Cat 11 the habenular nuclei were destroyed by the large lesion shown in Fig. 1, A and B, which extended laterally far enough to destroy the *centre médian* and damage the pars posterior of the lateral nucleus. It obliterated the caudal end of the third ventricle. Only the most ventral part of the zone of transition between the hypothalamus and the tegmentum of the mesencephalon was left intact.

By far the greatest damage was done in the last 3 cats of group B. In Cat 13 all of the medial portion of the thalamus was destroyed from the level of the anterodorsal nucleus backward to the border of the superior colliculus. The dorsomedial, habenular and parafascicular nuclei were destroyed bilaterally as were also the posterior commissure and the nucleus in the laterally spreading fibers of the posterior commissure, sometimes called the nucleus of the posterior commissure. All of the nuclei of the midline were either destroyed or greatly atrophied, and due to their disappearance and the absence of the dorsomedial nucleus the dorsal part of the third ventricle was greatly enlarged (Fig. 1, C). The walls of the third ventricle were badly damaged at the level at which it joins the cerebral aqueduct (Fig. 1, D).

In Cat 14 the damage began immediately behind the three anterior nuclei. There was bilateral destruction of the dorsomedial and other midline nuclei and also of the habenular and parafascicular nuclei. The nucleus in the laterally spreading fibers of the posterior commissure was destroyed on one side but intact on the other. The caudal part of the posterior commissure was intact. The lesion extended lateral-ward on both sides destroying the *centre médian* and damaging the pars posterior of the lateral nucleus. On one side it extended ventrally to the surface of the field H of Forel while on the other the nucleus subparafascicularis was intact.

In Cat 15 the damage extended forward to the anterior thalamic nuclei. The dorsomedial, parafascicular and habenular nuclei were destroyed bilaterally. The nucleus in the laterally spreading fibers of the posterior commissure was destroyed on one side, but almost intact on the other. The anterior half of the posterior commissure was destroyed. The parafascicular nucleus and the *centre médian* were destroyed bilaterally. The pars arcuata of the ventral nucleus and the pars posterior of the lateral nucleus were extensively damaged. The damaged area extended ventrally to within a short distance of the fields of Forel.

Discussion

The medial nuclei of the thalamus which were completely or nearly completely destroyed in the last 3 cats are the ones most intimately associated with the hypothalamus and it would be to them that one would look for any control which the thalamus might exert over body temperature.

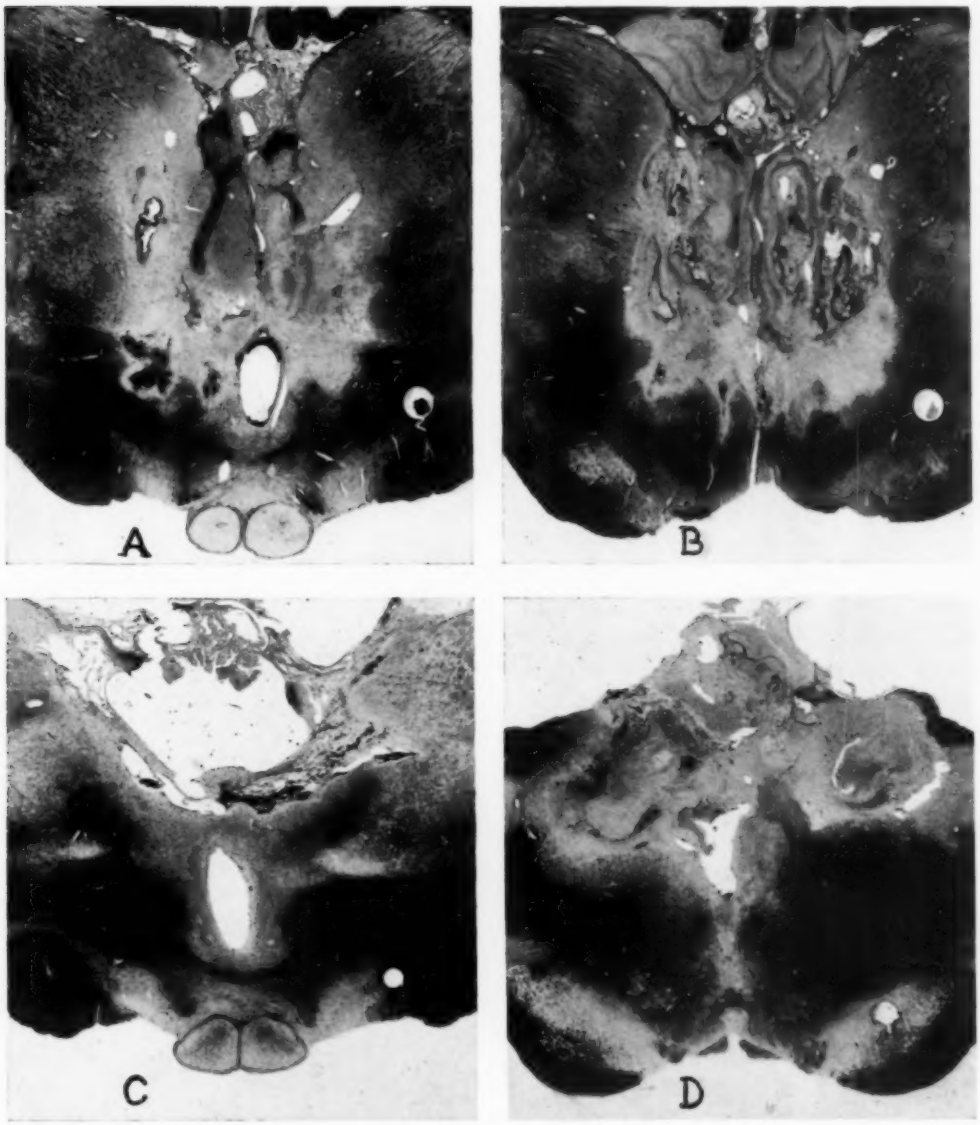

FIG. 1. A and B represent photomicrographs from transverse sections of the brain of Cat 11 at the level of the lower border of the mammillary bodies (A) and at a level slightly caudal to the mammillary body (B). C and D represent photomicrographs from transverse sections of the brain of Cat 13 at the level of the mammillary body (C) and at the level of the third nerve (D).

The lateral nuclei which serve to relay impulses to the cerebral cortex would not be likely to be concerned in temperature regulation. Moreover decorticate cats in which the lateral thalamic nuclei had been removed or had undergone degeneration regulated body temperature in an apparently normal manner although they were more inclined to shiver than normal cats in a

cool environment (Pinkston, Bard and Rioch, 1934; Bard and Rioch, 1937). These decorticate cats panted when they became overheated.

There would seem, therefore, to be no reason to attribute any essential part of temperature regulation to the thalamus if it were not for the observations of Lilienthal and Otenasek (1937) who found that the polypneic panting, which occurs in acutely decorticate cats, was not abolished by removal of the hypothalamus to the level of the caudal border of the mammillary bodies so long as the caudodorsal part of the thalamus remained intact. Removal of this part of the thalamus abolished panting. On the basis of these observations they postulated the existence of a center for polypneic panting in "the caudodorsal portion of the thalamus, an area which lies below the habenular complex and surrounds the anterior part of the iter." But, since our Cats 11, 13, 14 and 15 in which this part of the thalamus was destroyed, panted in a normal manner in hot box tests and showed typical polypneic panting when decorticated, it cannot be said to contain a center which is essential for panting.

Special interest attaches to Cat 11 which as shown in Fig. 1 B had lesions that left only the most ventral part of the zone of transition between the hypothalamus and mesencephalic tegmentum intact. Farther forward the fields of Forel were destroyed but the region dorsolateral to the mammillary bodies was bilaterally intact (Fig. 1 A). The fact that this cat was not somnolent and showed no disturbance in temperature regulation is to be attributed to the integrity of these regions. It has been shown that lesions dorsolateral to the mammillary bodies cause somnolence in the monkey (Ranson, 1939), catalepsy in the cat (Ingram, Barris and Ranson, 1936) and marked disturbances in temperature regulation in the monkey (Ranson, Fisher and Ingram, 1937) and in the cat (Clark, Magoun and Ranson, 1939). The figures published in these papers show that the lesions were often not confined to the region dorsolateral to the mammillary bodies but extended dorsally into the fields of Forel and even into the thalamus proper. The results obtained on Cat 11 supplement those in the earlier experiments and show that these more dorsal parts may be destroyed without causing these symptoms. The absence of these symptoms in this cat is to be explained by the fact that it is through the region dorsolateral to the mammillary bodies that the chief part of the descending path from the hypothalamus runs (Ranson and Magoun, 1939).

Summary

Damage to the thalamus causes no obvious disturbance of temperature regulation.

The caudodorsal portion of the thalamus does not form an essential part of the mechanism responsible for panting.

At the level of and just caudal to the mammillary bodies the descending paths from the hypothalamus which are concerned with temperature regulation lie near the ventral surface of the brain.

REFERENCES

BARD, P., and RIOCH, D. McK. A study of four cats deprived of neocortex and additonal portions of the forebrain. *Bull. Johns Hopk. Hosp.*, 1937, *60:* 73–147.

CLARK, GEORGE, MAGOUN, H. W., and RANSON, S. W. Hypothalamic regulation of body temperature. *J. Neurophysiol.*, 1939, *2:* 61–80.

INGRAM, W. R., BARRIS, R. W., and RANSON, S. W. Catalepsy, an experimental study. *Arch. Neurol. Psychiat., Chicago*, 1936, *35:* 1175–1197.

KLEYNTJENS, FRANÇOIS. Some factors influencing thermal panting in the cat. *Amer. J. Physiol.*, 1937, *119:* 352.

LILIENTHAL, J. L., JR., and OTENASEK, F. P. Decorticate polypneic panting in the cat. *Bull. Johns Hopk. Hosp.*, 1937, *61:* 101–124.

PINKSTON, J. O., BARD, P., and RIOCH, D. McK. The responses to changes in environmental temperature after removal of portions of the forebrain. *Amer. J. Physiol.*, 1934, *109:* 515–531.

RANSON, S. W. Somnolence caused by hypothalamic lesions in the monkey. *Arch. Neurol. Psychiat., Chicago*, 1939, *41:* 1–23.

RANSON, S. W., FISHER, C., and INGRAM, W. R. Hypothalamic regulation of temperature in the monkey. *Arch. Neurol. Psychiat., Chicago*, 1937, *38:* 445–465.

RANSON, S. W., and MAGOUN, H. W. The hypothalamus. *Ergebn. Physiol.*, 1939, *41:* 56–163.

TEAGUE, R. S., and RANSON, S. W. The role of the anterior hypothalamus in temperature regulation. *Amer. J. Physiol.*, 1936, *117:* 562–570.

EFFECTS OF FRONTAL LOBE LESIONS ON TEMPORALLY ORGANIZED BEHAVIOR IN MONKEYS*

JOHN L. FINAN

From the Department of Psychology and Laboratory of Physiology, Yale University, New Haven, and the Psychological Laboratory, St. John's College, Annapolis, Maryland

(Received for publication January 24, 1939)

RECENT interpretations of frontal lobe function have made use of the concepts of "synthesis"[3] and "temporal organization" (serialization) of behavior,[19,25] and the evidence warrants recognition of some such principle of associative connection. Many agree, however, that further analysis will require fractionation of these descriptive concepts into experimentally workable and verifiable hypotheses. The investigations of Jacobsen[17–25] have served this end by contrasting performance of monkeys in the delayed response test, which is lost after bilateral ablation of the frontal areas, with that of simple discrimination learning, which is retained. Jacobsen points out that an essential difference between the two kinds of performance lies in the absence of differential sensory cues in the delayed response situation. The present investigation was designed to test in other situations the validity of this difference.

Two problems involving temporal discrimination have been studied. These tasks possess, in common with the delayed response tests, the absence of immediate stimulus cues to which the subjects can respond. The *first* problem involved use of an observation box divided by a falling door into two chambers equipped with "punishment" grilles. The animal, placed in a compartment, was forced by appropriately timed electrification of the two grilles, to remain for a fixed period of 10 sec. after the elevation of the door, and to cross into the opposite compartment during a subsequent 11 sec. interval (Fig. 1). The subject was thus trained to respond in the safe interval between the premature and tardy punishment intervals. The *second* technique employed a simple rectangular maze consisting of alternative pathways to food, different in the sole respect that one side entailed a longer time of enforced detention than the other (Fig. 2). Training on this problem was continued according to a method which eliminated nontemporal cues until the animals showed a stable preference for the side of shorter confinement.

Loss of temporal discrimination habits following operation would ally the behavioral and neural processes of these adaptations with those of delayed response performance, and indicate that the absence of differential cues is the responsible factor. Postoperative retention of these habits, on the other

* A dissertation submitted to the Graduate School, Yale University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June 1937.

hand, by demonstrating that frontal lobe ablation affects delayed response and temporal discrimination habits selectively, would indicate the existence of separate behavioral processes mediated by independent neural mechanisms. In addition, the problem of whether or not "serialization," or the "temporal organization of behavior," may validly be regarded as the per-

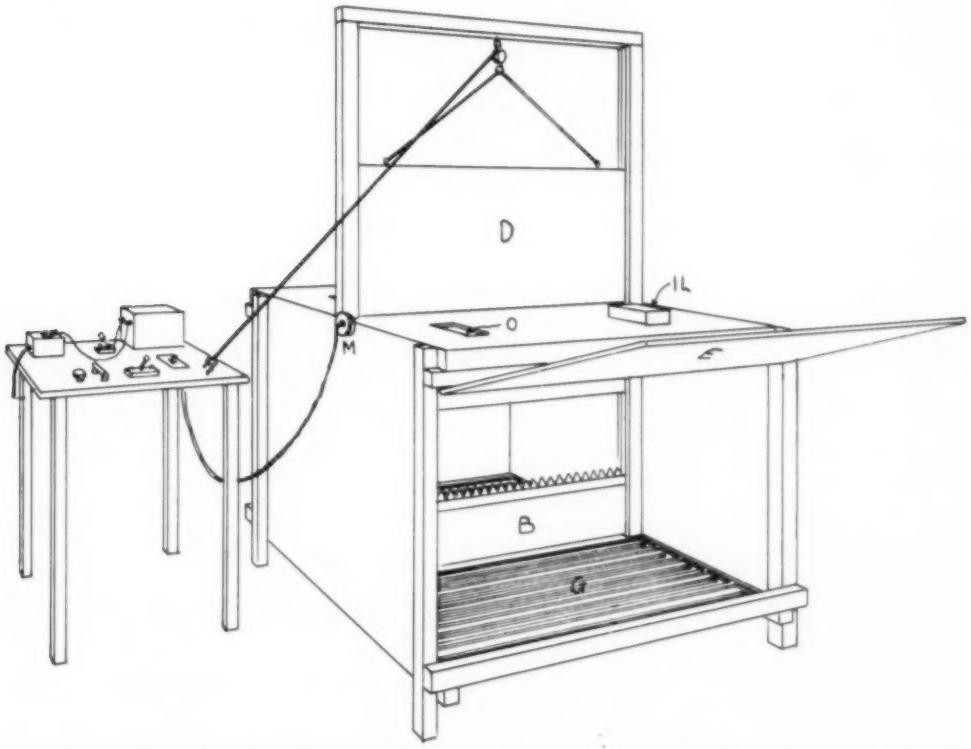

FIG. 1. Diagram of shuttle-box used in temporal discrimination training. The box (dimensions, 152 × 91 × 76 cm.) was divided into two equal compartments by a portcullis door (D) which rested, when lowered, on a sheet iron door-sill (B) 25 cm. in height. The floor was constructed of 3 mm. iron strips 12 mm. wide, and with a 30 mm. separation, alternately connected to form two independent circuits on either side of the central barrier (B). Both shock-systems were supplied with 110 V. 60 c./sec. current reduced by a 100,000 Ω variable resistor and a 24,000 Ω fixed resistor in series. Observation of the animal's behavior was accomplished by means of illumination (IL) and observation (O) apertures, the latter being covered with one-way vision glass. Manual controlling devices were mounted on a table-top adjacent to the apparatus.

formance mechanism lost after ablation of the frontal areas, would be critically answered.

EXPERIMENTAL METHODS AND SUBJECTS

Shuttle-box. An observation box was employed similar in principle to one used by F. L. Ruch[39] and by Dunlap and Gentry[5,11] in discrimination studies with white rats (Fig. 1). It was essentially a chamber divided into two compartments by a communicating doorway through which the animal could pass from one side to the other. The interior of the chamber offered no overhanging surfaces on which the animal might support itself to

escape shock. A current of approximately 0.001 A. was found adequate to meet the behavioral requirement of shock without unduly exciting the animals. Raising the door by means of a pulley system constituted the signal stimulus. Another stimulus beginning with the opening of the door was a weak tone obtained by impressing a 60 c./sec. 110 V. current across a speaker unit which fitted into the wall of the box in a central position.

To respond correctly in the shuttle-box, the animal must move from the initially occupied compartment to the opposite side during an 11 sec. interval beginning 10 sec. after the onset of the signal stimulus. A trial consisted of an interval of 35 sec. initiated by the opening of the portcullis door and the onset of tone. Lowering of the door together with the cessation of tone ended the trial. A correct response was scored when the animal arrived on the opposite grille not earlier than 10 sec. and not later than 20 sec. after the door was raised. Premature responses, earlier than 10 sec. were punished with shock on the opposite or "contralateral" grille, and failure to respond before the 20th second was punished by shock on the same or "ipsilateral" side. Response-latencies were measured with a stop-watch to the nearest fifth second, and a description of the motor-pattern of response was recorded. A work-session consisted usually of 20 trials.

The following *control* procedures were observed. Training was conducted as nearly as possible at the same time on successive days. A variable daily period of adaptation was allowed the animal upon introduction to the box. To insure the resumption of a quiescent posture in preparation for the next trial, trials were separated by short periods of time varied in duration to avoid conditioning to the inter-trial interval. It is unlikely that periodic or progressive sounds served as cues inasmuch as incidental noises which occurred in the environment were variable and did not appear to influence the behavior of the animals. Apparatus cues were made impossible by throwing the switch controlling the opposite grille only after the animal had responded. Intentional variation in the posture and movements of the experimenter did not alter the established response. An additional control of secondary cues is afforded by the fact that behavior remained unchanged when the controls were manipulated by other experimenters.

The establishment of the correct "shuttling" habit was accomplished in two stages. The simple habit of crossing to the opposite compartment in response to ipsilateral shock following the onset of the signal stimulus was first built up. Later training developed the correct timing of the response during the safe interval. During the preliminary training, door-tone stimulation was followed by the ipsilateral shock beginning at the 3rd sec. and continuing until the 20th sec. in the event the animal did not cross sooner. The onset of this shock was gradually dropped back from the 3rd to the 20th sec. When anticipatory crossing occurred with some regularity this mode of training was discontinued to avoid fixating the simple response which tended to creep forward in time to the signal stimulus. In the later training, the ipsilateral shock was activated from the 20th to 25th sec. the contralateral shock from the 1st to the 10th sec. Training was continued until the animals attained a stable level of approximately 80 per cent correct responses in 200 trials.

Temporal discrimination maze. The apparatus (Fig. 2) is an adaptation of a maze employed by Sams and Tolman[40] in discrimination studies in white rats. It consisted of two equidistant, alternative pathways to a food chamber with detention-doors allowing controlled confinement periods in the two pathways. The first of the routine five daily trials began with the raising of doors A and B and the unlocking and raising of door E. From the choice-point the animal was free to pass under either door, the chosen door being lowered immediately to form a closed detention-chamber with door C or D. The criterion of a choice consisted of the animal's entering a detention-chamber far enough to permit safe closure of the door. After the lapse of the 30 or 120 sec. time interval, door C or D was opened along with gate F admitting the animal to the food-chamber where it found a slice of banana. In preparation for the next trial, the entrance and food cages were then exchanged without removing the animal. To eliminate the possibility of response to a quicker return to the starting position after the correct response, cages were not intersubstituted until 4 min., including detention-time, had elapsed since the beginning of the trial. A control of secondary cues was provided by the fact that other observers were able to manage the apparatus without alteration in the subjects' performance.

Following an initial 24 hr. habituation period the preferred side was determined for each animal by five runs made with the two routes temporally equal at 30 sec. detention. The non-preferred side (chosen 0–1 times) was then selected to be the 30 sec. detention-

route, while the preferred side (chosen 4–5 times) was made the 120 sec. pathway. When the initial preference had been broken down and the temporally shorter route chosen with the frequency demanded by the criterion of 15 correct responses in 20 trials, the formerly shorter side was made the longer. Under these reversed conditions training was continued until the criterion was met a second time. For the animals operated before training, this point marked the end of the experiment. The normal animals were, at this time, subjected to operation and subsequently brought to the previous degree of mastery with the detention-intervals in the same right-left relationship as before operation. The relationships were again reversed and the animals forced to meet the criterion for the fourth time.

Delayed response. The delayed response control experiment served as a behavioral verification of the extent of lesions, as well as an additional proof that these particular animals were, in accordance with Jacobsen's general findings on animals without frontal areas, incapable of correct response in this situation. For an exact account of the apparatus and method, the reader is referred to Jacobsen's description[20]. Briefly, the animals were shown in which of two drawers a slice of banana was concealed, and after intervals varying from 0–30 sec. a door was raised allowing the subject to leave a confinement chamber to

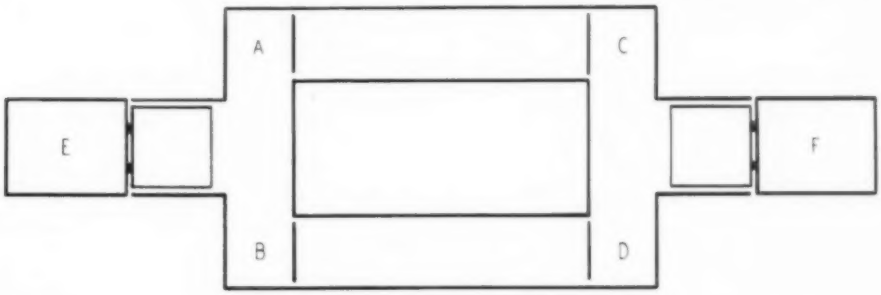

FIG. 2. Floor of temporal discrimination maze. With the exception of wire cages E and F, the maze was constructed of wood covered on the superior surface with hardware cloth. The lengths of the various units were as follows: entrance and exit alleys 30 cm.; choice and exit chambers 120 cm.; detention chambers 132 cm.; the apparatus was uniformly 41 cm. in height. Doors (A, B, C and D) were controlled remotely by pulley ropes which terminated behind a one-way vision screen at the front of the apparatus.

choose between the drawers. Following habituation to the apparatus, a series of test trials was run. The reward was presented on the right or left in chance order. Trials involving no delay were frequently interspersed among the test trials in order to avoid excessive frustration from repeated failure.

Subjects. Four immature mangabey monkeys (*Cercocebus torquatus atys*) served as subjects. They were housed in large cages and fed on a standard laboratory diet. Regular monthly weighings indicated, with one exception, that the animals maintained a normal state of health throughout employment. Details concerning animals may be found in the appendix.

Surgical and anatomical procedures. The objective of the operations was the complete removal of the frontal association areas, shown by Jacobsen and collaborators[23] to be essential for delayed response performance. This region includes the frontal pole and lies lateral to the frontal sulcus, extending posteriorly to the arcuate sulcus. Actually the attempt was made to remove all tissue corresponding to Brodmann's[4] areas 9-10-11-12, sparing area 8 (eye-fields) by extending the lesion along an imaginary line projected from the inferior limb of the arcuate sulcus to the longitudinal fissure. Operations were carried out in both one and two stages.* Aseptic precautions were observed throughout. Tissue was incised with the Davis-Bovie electrosurgical knife and removed by blunt dissection, whenever

* The author is greatly indebted to Drs. J. F. Fulton, C. F. Jacobsen and A. E. Walker for surgical assistance. For a detailed description of the surgical procedures see Fulton and Keller.[10]

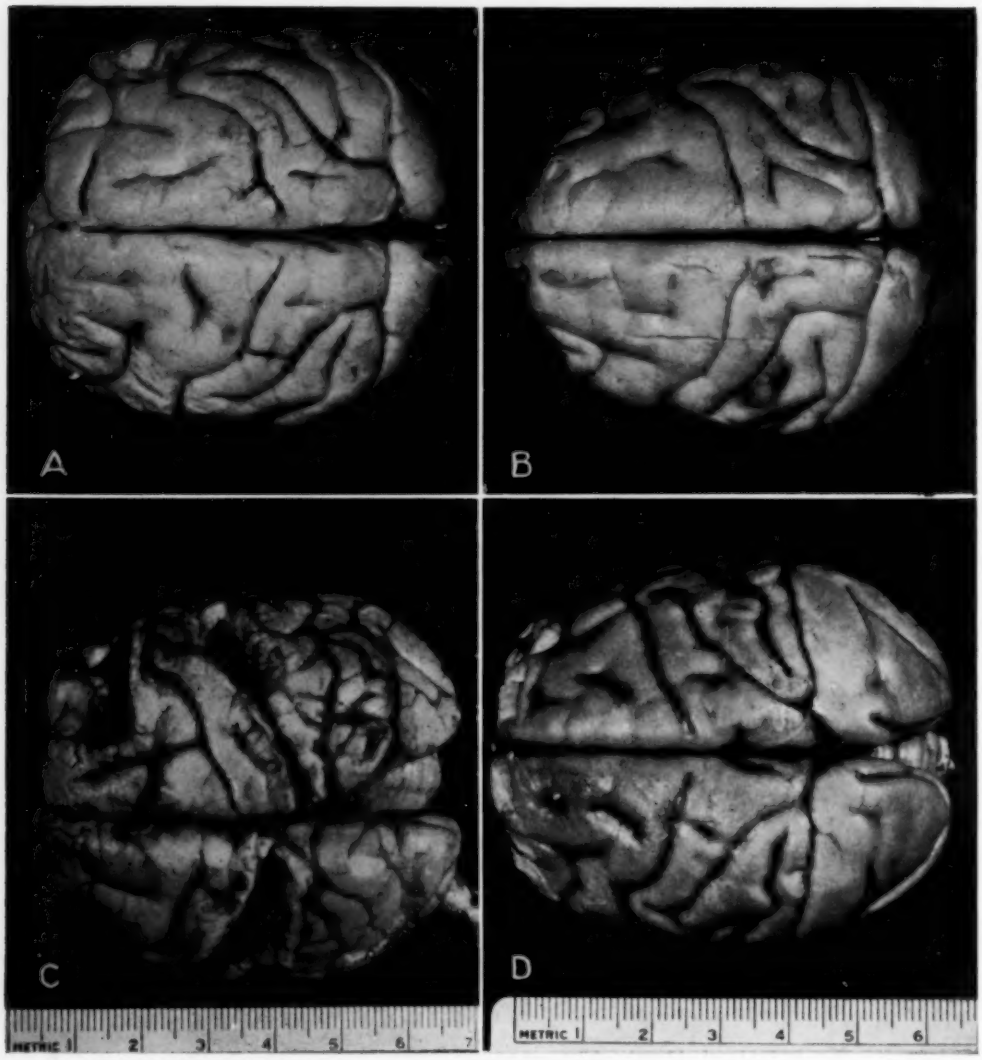

FIG. 3. Photographs of brains at autopsy showing extent of lesion. A. Expt. 1 (Frontal 40). B. Expt. 2 (Frontal 41). C. Expt. 3 (Frontal 42). D. Expt. 4 (Frontal 43).

possible in one piece. On completion of the postoperative tests, the animals were sacrificed and brought to autopsy. The brains were fixed by formalin injection. Lesions were reconstructed from three sources: (i) the drawing of the operative field and lesion traced on cellophane at the time of operation, (ii) histological examination of the extirpated block, and (iii) careful gross examination of the brain removed at autopsy.

RESULTS

Shuttle-box

Training period. Two animals, Experiments 1 and 2 (See Appendix), successfully mastered this problem to the 80 per cent criterion. The simple

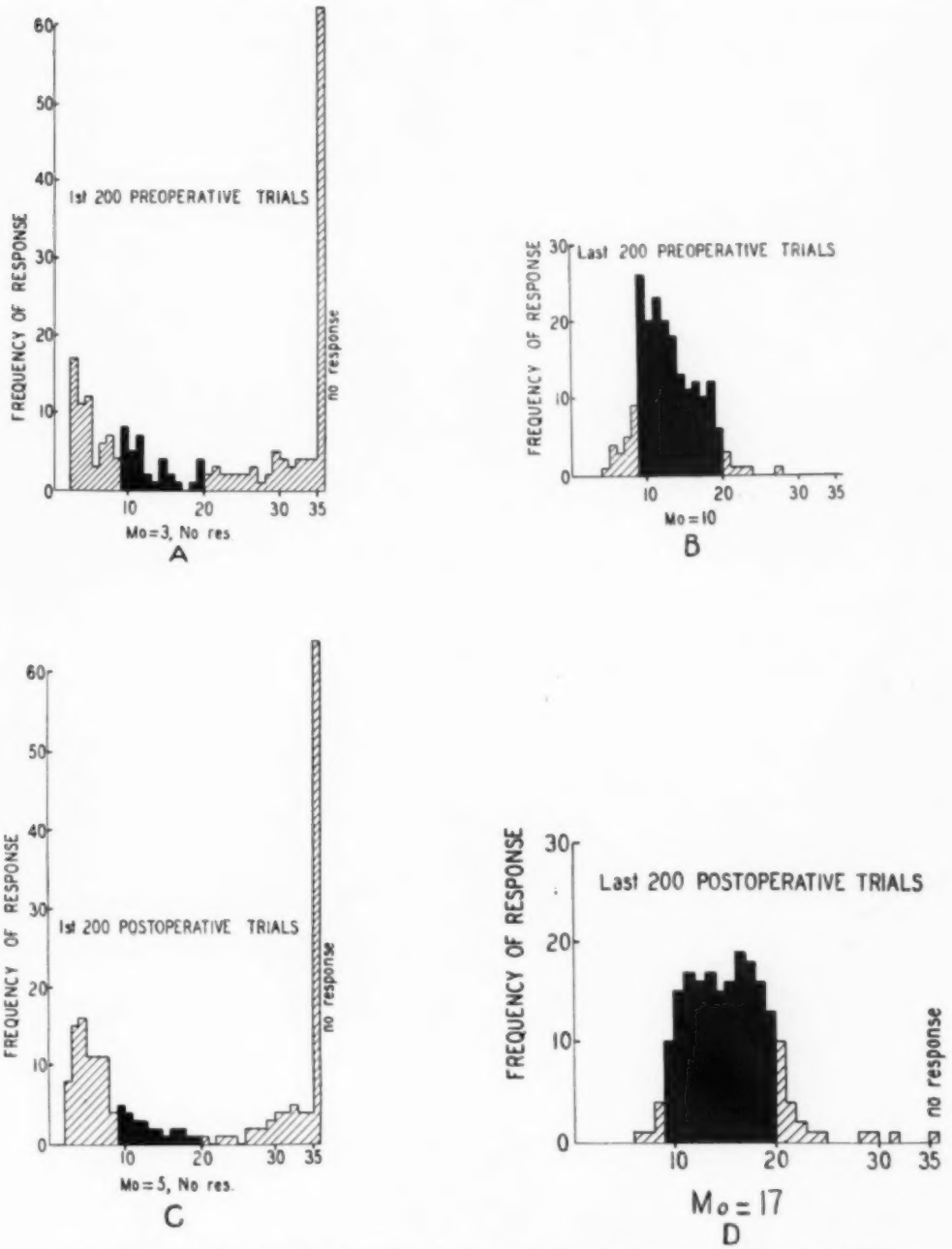

FIG. 4. (Expt. 1). Summary of results with shuttle-box. Frequency distribution of response-latencies for each sec. of the 35 sec. interval.

crossing habit, described in the procedure, was established in 14 trials in Experiment 1 and in 20 trials in Experiment 2. In the course of the following 49 trials of Experiment 1, and 20 trials of Experiment 2, the beginning of

the shock was dropped back gradually from the 3rd to the 20th second. In order to avoid fixation of a habit of premature response, the contralateral shock was then introduced. In spite of the fewer trials required in Experiment 2 in learning to cross, the resultant behavior under the double shock condition was the same for both subjects and consisted regularly of alternate anticipatory crossing and complete failure to respond. During the first 200

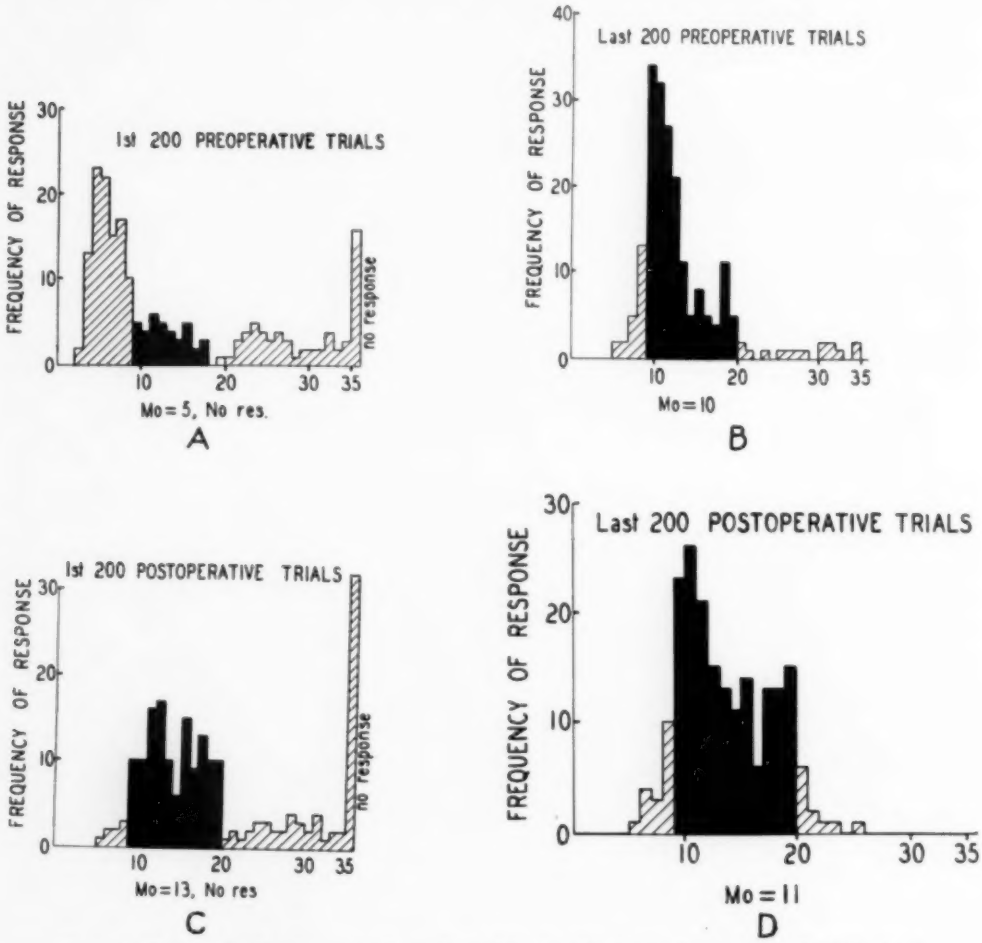

FIG. 5 (Expt. 2). Summary of results with shuttle-box. Frequency distribution of response-latencies for each sec. of the 35 sec. interval

trials, represented in Fig. 4A and 5A, modal responses for both animals fell into two groups; one with a central tendency early in the 35 sec. interval probably resulting from the initial short-delayed conditioning, the other with a maximum value at "no response" probably resulting from the introduction of contralateral shock. Both types of response appeared to depend on the immediately preceding errors. With continued training under the same conditions, the modal response assumed a position intermediate be-

tween these two extremes of anticipation and tardiness until, in the last 200 preoperative trials, both animals responded most frequently at the earliest safe point. Comparison of Fig. 4B and 5B demonstrate the consistency of response-latencies.

The course of acquisition of the habit is plotted for both animals in Fig. 6 in which each point of the curve represents the percentage of correct responses for successive hundreds of trials. The curve of acquisition for Experiment 1 indicates chance performance during the first 800 trials, rising sharply during the next 100 trials to maintain a stable level of slightly more than 80 per cent. The course of learning in Experiment 2 rides somewhat less

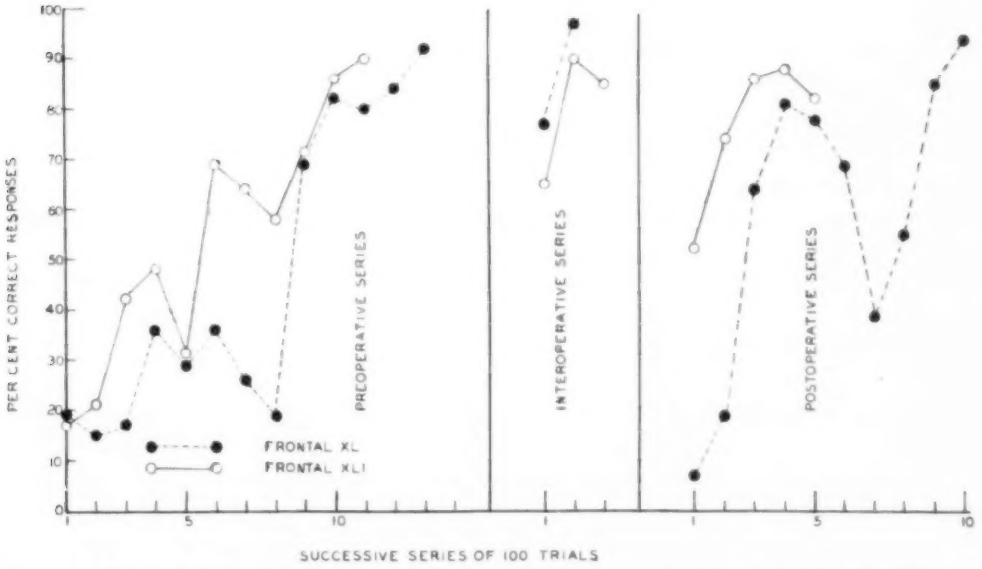

FIG. 6 (Expts. 1 and 2). Summary of preoperative and postoperative training in shuttle-box, showing percent correct responses for successive series of 100 trials.

sharply in roughly cumulative peaks until a stable level of 86 per cent correct responses was achieved. Behavior in the apparatus appeared to parallel the degree of mastery indicated by the quantifiable aspects of response. With the appearance of the correct habit, both animals substituted for the earlier habit of passive waiting, a marked activity which consisted of repeatedly approaching and retreating from the barrier, and circling around the chamber. These movements diminished perceptibly in frequency and amplitude with the immediately approaching safe-interval, and usually terminated in an abrupt halt at the barrier which was then crossed slowly and cautiously.

Interoperative retention. Figure 6, describing the course of retention after unilateral frontal lobectomy, indicates that the preoperative level of mastery was surpassed and averages of 87 and 88 per cent correct responses stably maintained for Experiments 1 and 2. Both animals tended to respond

3 sec. later in the safe interval than previously. In addition the distribution of responses during the entire safe interval was more equitable than in the earlier trials. Data obtained from the two animals were consistent in demonstrating that left unilateral ablation of the frontal areas caused no impairment in the accuracy of response to a temporal interval.

Postoperative retention. For 3 weeks following the second operation, Experiment 1 failed to show correct response to stimulation in the apparatus, while within a week postoperatively, Experiment 2 responded with a degree of accuracy equivalent to that of the preoperative criterion. The slump in performance in Experiment 1 immediately after operation (Fig. 6) can probably be considered the result of infection; first, because of the coincidence of the affliction and the impairment of the habit, and second, because of the absence of a similar effect in Experiment 2 which was uncomplicated.

A period of "no response" well marked in the immediate postoperative behavior of both animals (See Fig. 4C and 5C), was supplanted by a short period of anticipatory crossing similar to that of the original learning. A third phase was characterized by multiple crossing during a single trial; after responding correctly, the animals shuttled between compartments as many as two to seven times before the door was lowered ending the trial. Occurring immediately after the second operation with a frequency of nearly 100 per cent, the number of repeated crossings diminished with progressive training without ever dying out completely. No comparable behavior had been observed during the preoperative training of either animal.

The criterion was surpassed in Experiment 2 during the second and third hundred postoperative trials and was stably maintained. In Experiment 1 the attainment of 79 per cent correct responses for the fourth and fifth hundred postoperative trials was followed by a slump in performance. It will be seen from Fig. 6 that the criterion was met postoperatively a second time during the 9th and 10th hundred postoperative trials. This inversion in the retention curve illustrates a type of variability well known in operated animals. A similar phenomenon has been reported in conditioning studies on normal human subjects[14]. The latencies of the last 200 responses, described in Fig. 4C (Experiment 1), were scattered with a slight preponderance of crossings late in the safe-interval. Figure 5D (Experiment 2) shows that the modal response fell somewhat earlier with a less equitable distribution of responses over the safe-interval. The general tendency for correct responses to occur at any point within the safe-interval correlates roughly with progressive training in both subjects.

Prior to the operation, the typical mode of response during the period of mastery consisted of several circlings around the box, terminated by a rapid succession of waverings close to the barrier. The complete inactivity immediately following frontal lobectomy was supplanted by a violent activity. During the last of the postoperative training, however, movements were almost entirely confined to the region of the barrier, where the animal picked at the grids, screws and other exposed parts of the apparatus. Move-

ment, then, in accordance with the findings of Wendt,[43] tended to vary in locus and amplitude, remaining fairly constant in frequency throughout training.

In summary, seriatim bilateral extirpation of the frontal areas in the two monkeys was not followed by permanent loss of ability to respond correctly to a temporal interval as presented in the shuttle-box problem.

Temporal discrimination maze. Four animals were used in this problem. Experiments 3 and 4 included preoperative training with later testing for postoperative retention. In Experiments 1 and 2 training in the problem for the first time was conducted after operation. Following 5 preference trials the problem in Experiments 3 and 4 was mastered to the criterion of 15/20 trials. The detention ratio of the two sides was then reversed and the reversal learned to the same degree of mastery. A quantitative account of the training appears in Table 1. Motivation was consistently higher in Experiment 4 than in Experiment 3, although with continued daily training, the maze was run in the latter with a minimum of dallying at the entrance and choice-points.

Table 1. Summary of preoperative and postoperative results on the temporal discrimination maze showing the number of trials and errors in each series to reach a criterion of 15/20 trials correct (criterion trials included).

Training series	Frontal 42		Frontal 43		Frontal 40		Frontal 41	
	Trials	Errors	Trials	Errors	Trials	Errors	Trials	Errors
PREOPERATIVE								
First series	91	52	50	21				
Reversal series	41	26	109	78				
POSTOPERATIVE								
First series	17	2	16	1	25	9	65	34
Reversal series	39	20	30	13	70	44	35	15

In the postoperative testing series, the completeness of retention was demonstrated by the absence of errors (Table 1). The possibility that merely a position-habit had been retained rather than the capacity to respond differentially to temporal intervals was controlled by running a subsequent reversal series which was mastered in Experiments 3 and 4 as indicated in Table 1. The fact that during the postoperative retention series in Experiment 4 the food-reward was invariably refused, emphasizes "escape" over the food motive in the solution of this problem. Resultant differences in the manner of response manifested in increased loitering and inactivity at the choice of exit points, in no way altered the accuracy of this animal's performance. The problem-attitude and manner of solution in Experiment 3 appeared to be unaffected by operation. In Experiments 1 and 2 the counter-preference series was mastered to the criterion, following which the same norm was reached under reversed conditions (Table 1). It merits mention that the operated animals learned this problem with somewhat greater ease than the normal animals.

Delayed response

Three animals served as subjects. Experiment 4 was run preoperatively with delay intervals ranging between 0 and 20 sec. The percentage of correct responses at each interval, presented in Table 2, show that this subject was entirely capable of correct choice within the limits tested. Postoperative retention tests on the same animal yielded results in substantial agreement with those reported by Jacobsen.[20] The interposition of even the smallest delays resulted in failure to respond with better than chance scores, although visually oriented response involving no delay was entirely possible (0-delay trials, Table 2). Continued daily tests allowing optimal opportunity for correct response showed no improvement in the performance of this task. Errors were variable and showed no consistent tendencies other than transitory position habits. The subject was frequently distracted and often retreated to the rear of the cage, refusing to work.

Table 2. Summary of the preoperative and postoperative training on delayed response.

Experiment	Period of Delay in Seconds					
	0	2	5	10	20	30
No. 4. PREOPERATIVE TESTS						
No. of trials	71	3	2	76	24	11
Per cent correct	91	100	100	92	83	100
No. 4A. POSTOPERATIVE TESTS						
No. of trials	166	11	119	87		
Per cent correct	92	37	58	53		
No. 1. POSTOPERATIVE TESTS						
No. of trials	369	183	244			
Per cent correct	83	52	58			
No. 2. POSTOPERATIVE TESTS						
No. of trials	187	90				
Per cent correct	83	49				

The remaining two animals were trained in delayed-response for the first time after operation. (In Expt. 1, 796, and in Expt. 2, 277 trials were run.) Table 2 indicates that both subjects were unable to master the delayed response problem after bilateral removal of the frontal areas. When visual cues were allowed (0 sec. delay), a high level of correct response was obtained in Experiment 1. With delays of 2 and 5 sec. results were only slightly above chance. On the trials involving no delay for Experiment 2 response was well above a chance level, dropping to 50 per cent when a 2 sec. delay was employed. Attempted solutions were extremely variable and seemed to manifest no systematic tendencies other than the occasional position preferences already described for Experiment 4.

Summary.—Results using 4 monkeys on 2 different temporal discrimination problems agree in indicating that neither unilateral nor bilateral lesions

of the frontal association areas cause impairment in the capacity to learn or retain the habit of responding correctly to temporal intervals. In contrast with these habits, the delayed response performance was permanently impaired by the same cortical injuries. The results presented here thus contain two kinds of evidence relevant to the effects of lesions of the frontal association areas on complex adaptive habits of a superficially related order and complexity.

Interpretation

The complex behavioral changes resulting from bilateral frontal injury in human patients cannot easily be forced into any single conceptual formula. The hypotheses of "association,"[2] "synthesis,"[3] "temporal organization,"[19,25] "active inhibition"[1,16] and "facilitation"[12] represent independent attempts to unify the variable symptoms of the frontal lobe syndrome, all falling short of scientific analysis because of their failure to define critical experimental alternatives. When, however, methodological differences are weighed, and adequate account taken of the sources of clinical error, the sum of both clinical and experimental evidence suggests that the situations which disclose frontal lobe deficit are predominantly those in which external stimulus control is at a minimum. Goldstein[12] reports a patient who was perfectly capable of rearranging small sticks into a roof-top angle a half minute after initial presentation, but who failed when required to reproduce the same angle pointing upward. According to Goldstein's analysis of this difference in performance, correct response was possible in the first instance because the stimulus relationships were apprehended as a *concrete* item of the patient's past experience, whereas, in the second case, it was necessary that the sticks be arranged as representative of a more abstract situation not encountered in previous experience. Summarizing the symptomatology of frontal lobe lesions, Goldstein notes that:

> "(the patient) is incapable of recollection when he is asked to recall things that have nothing to do with the given situation. But when it is possible to put him into a situation to which the material inquired for belongs, recollection appears suddenly . . . he is able to learn new facts; he may be able to learn numbers, syllables, or movements by heart; he is able to hold in memory situations, facts of environment, etc., but he is able to reproduce these only in the same situation in which he has learned them. . . . Therefore the patient's performance consistently varies according as the task is embedded in a concrete or abstract situation" (12, pp. 36–37).

The interpretation of Brickner in terms of "synthesis" and that of Penfield and Evans[38] as a loss of capacity for "planned administration," are compatible with Goldstein's emphasis on the non-sensory character of those situations which reveal loss of adaptive function in cases of frontal lobe involvement.

The absence of differential cues proves to be the factor common to the more exact experimental situations which demonstrate behavioral changes in animals after ablation of the frontal areas. The following tests employed by Jacobsen to demonstrate frontal lobe deficit all show the same lack of

external stimulus support: (i) Instrumentation tests[25] in which a chimpanzee is presented with food and a stick necessary for drawing it in at opposite ends of a cage. Here the elements of correct solution may not be united in a single perception, but must be supplemented either by memory of the stick, or of the food on the unseen platform. (ii) Serial reaction studies[25] involving the possibility of two types of errors, namely those of serial order (anticipation) in which spatial cues were available, and those of direction of movement, in which they were absent. The learning of the sequence of response was much more rapid than that of appropriate direction. Response was markedly less successful when dependent on the inward or outward movement of a particular peg mediately associated with food. (iii) The delayed response technique[19,20,23] requiring differential response after enforced postponement, likewise eliminated differential sensory cues, since the paired aspects of the situation lend no clue to the correct response at the moment of choice. (iv) The delayed alternation situation[24] in which the absence of differential cues is expressed in the fact that correct response can occur only with reference to the immediately preceding response. The impaired performance obtained in these four situations stands in sharp contrast with the excellent retention or learning of problem boxes and discrimination problems in which the cues necessary to correct response are part of the immediate test situation.

On the basis of this evidence, Jacobsen has proposed that: "The peculiar contribution of the frontal association areas (appears to be) . . . the recall of a particular past event which may be only in mediate association with some aspect of the present environment, and the integration of recalled elements with the organism's stable habit systems" (20, pp. 55–56). As employed by Jacobsen, the concept of immediate memory implies a distinction, based on the dependence of certain types of performance on differential stimulus cues, between "retentive" or "associative" memory, and the fundamentally different kind of organization operative at the level of the memory span.

In terms of the principles outlined above, it will be noted that the shuttle-box problem requires response to an "absolute" interval of time, *without external stimulus support,* after self-enforced postponement of response. The temporal discrimination maze demands a "relative" discrimination of alternative detention intervals *mediately associated* with briefer detention. These tests have in common with the delayed response test these essential features: response after the lapse of an interval of time, and *the absence of differential cues in or directly related to the test situations.*

While the temporal situations here employed are similar to the delayed response test in the absence of differential cues, the two kinds of problem are distinguishable in terms of their differential susceptibility to the effects of cumulative training. Assuming with Nissen that a fundamental difference between delayed response and discrimination learning lies in the fact that in the former "the animal is not trained to the correct response by making

it . . . but instead must respond on the basis of a single unrewarded and unpunished presentation" (24, p. 132), we can describe the distinctive features which enable the temporal and delayed response habits to be differently affected by cortical ablation in terms of habit-acquisition. Waiving possible genetic differences between the two types of behavior in favor of a description in terms of performance on a given trial, we are forced, since the essential characteristics of both hinge on the *absence* of differential external cues, to seek differences in their underlying central processes. An analysis of these differences awaits a more precise investigation of the behavioral and neural processes operative in the two kinds of solution. The present research thus provides new lines for the fractionation of the learning process into conditioned response fixation and non-trial and error solution previously proposed by Lashley,[29,30] Jacobsen,[20] Maier,[33,35] Krechevsky[27] and Harlow[13] on neurological grounds, and by Köhler[26] and Tolman[42] on the basis of behavioral evidence. Our results delimit the concept of immediate memory further by showing the necessity for qualifying Jacobsen's definition in terms of the absence of differential stimulus cues.

A related purpose of the investigation was to determine the possible role of the "trace" reflex as the mechanism of delayed reaction. To assume in advance that the two behavioral processes may be identified, lends the problem a clear and simple experimental formulation and is further justified by the theoretical expectation that the trace component in many complex habit sequences provides a basic unity on which the serial order of the action depends.[15,31,41] Results from the two temporal discrimination problems, however, clearly show that neither retention nor relearning of the "trace" reflex type is dependent on the integrity of the frontal areas. In the light of these findings, the "trace" reflex as an integrative mechanism of serial habit-formation does not appear to represent a unitary function and hence requires restatement in terms of the conditions under which it operates together with the exact properties which distinguish it from other types of organization.

In a similar connection, Jacobsen has suggested that in so far as such concepts of frontal lobe function as "serialization" and "synthesis" are tenable, they are reducible to immediate memory or to the "temporal organization of behavior" defined operationally in terms of the delayed response situation. He writes: "It would thus appear that bilateral lesions of the frontal areas seriously impaired adjustment to situations involving temporal organization of behavior. On the other hand, ability to manipulate several sticks as tools was evident when the materials were presented in a spatially organized field and did not require sustained temporal organization" (25, p. 3.) As Jacobsen[20] later points out it is questionable whether this formulation, although experimentally more useful than the broader notions mentioned above, does not likewise lack value as a tool of rigorous scientific analysis. From our results it appears that temporal organization as tested in the present experiments plays no essential role in delayed response per-

formance and hence cannot, without further qualification, be considered the mechanism of immediate memory.

Speculation concerning the differences in the behavioral and neural processes underlying the two types of performance distinguished as association (retention) and non-trial and error solution (immediate memory) has been kept at a minimum in the absence of more complete evidence. Our results, however, demonstrate that the problem of further fractionating the learning process is genuine rather than conceptual. An attempt has been made to outline some of the experimental variables necessarily to be encountered in future attempts at its solution.

Summary

The effects of removal of the frontal association areas of the cerebral cortex were studied in four monkeys with three types of behavioral tests, alike in the respect that differential cues were absent from the external situation, but different in respect of the degree of influence exercised by repeated training in the establishment of their corresponding habits. The tests were: (i) a temporal discrimination maze in which available sensory cues were mediately associated with the briefer detention of the correct pathway, (ii) a shuttle-box which required response to be made within a fixed interval after the onset of a signal stimulus, and in which, again, the cues necessary to correct performance must be supplied by the subject itself; (iii) the delayed response test in which the cues representative of immediately previous stimulation also had to be contributed by the animal.

The results are summarized as follows: *Unilateral* lesions of the frontal areas caused no impairment in performance on any of the three tests. *Bilateral* ablation of the frontal areas affected performance in different ways. (i) The ability to perform in a shuttle-box was retained without impairment. (ii) Retention of the maze test was not impaired, nor was the capacity to learn this task for the first time reduced. (iii) The capacity to respond correctly in the delayed response test was totally and permanently lost by the same subjects.

It is concluded that, although the frontal areas are essential to one type of centrally controlled behavior, these regions are not essential to other types of equally "representative" behavior investigated in this study. The concept of immediate memory is accordingly further qualified: (i) in terms of "associative" and "non-trial and error" learning, and (ii) in terms of discrete neural mechanisms underlying the two kinds of behavior.

The author wishes to acknowledge his indebtedness to Dr. Carlyle F. Jacobsen and Dr. Donald G. Marquis under whose joint direction the investigation was conducted, and to Dr. John F. Fulton in whose laboratory the work was carried out.

Appendix

The similarity of methods employed and the consistency of the results obtained allow individual protocols to be presented in brief form. Clinical records of these animals are published elsewhere[36,37].

Experiment 1—Bilateral ablation of frontal areas in two stages; retention of shuttle-box habit, abolition of delayed reaction, postoperative learning of temporal discrimination maze habit (Frontal 40).

The subject of this experiment was an immature female sooty mangabey (*Cercocebus torquatus atys*) weighing 1700 g. The animal had been observed for several months prior to training and was readily adapted to work. Its *preoperative* training (Dec. 2, 1935 to Mar. 9, 1936) was directed solely to the mastery of the shuttle-box.

First operation—Ablation of left frontal areas (March 9, 1936). A suitable anesthesia was obtained with Nembutal administered intraperitoneally. A generous bone flap was turned down exposing the left hemisphere. The dura was reflected and an attempt made to remove all tissue anterior to an imaginary line projected from the inferior arcuate sulcus to the mid-line. This included areas 8, and 9-10-11-12 of Brodman; area 6 was not encroached upon. The weight of the freshly extirpated block was 1.84 g. *Recovery* was uncomplicated by sensory or motor disturbances except for a transient object vision "hemianopsia" observed on the second postoperative day, involving the left temporal and right nasal fields. Circus movements toward the side of the lesion were noticed immediately following operation, passing away on the third day. Healing of the wound was rapid and the general state of health satisfactory.

Interoperative training (Mar. 10–17). Daily trials on shuttle-box were begun on the first day following operation and were continued for seven days. The preoperative level of mastery was maintained and even surpassed.

Second operation—Ablation of right frontal areas (Mar. 21, 1936). Under sodium amytal anesthesia the lesion made in the first operation was closely duplicated on the right side without alteration of the operative procedure. The extirpated block weighed 2.7 g. in the fresh state. Immediate *postoperative* recovery was complicated by a superficial scalp infection observed on the second day following operation. For the ensuing three weeks, the animal was depressed and without appetite. During this period no alterations in sensory or motor function were observed. With the recovery from infection, the animal became brighter, activity was more marked and the appetite strikingly increased over the normal preoperative level.

Postoperative training (Mar. 27–Dec. 7, 1936). Testing on the shuttle-box was resumed immediately after operation. Following a period of "no response" the animal regained its previous level of mastery. During the fifth postoperative month, delayed reaction training was undertaken but the animal was unable to master the problem. Later, in the ninth month, training was conducted in the temporal discrimination maze habit, which the animal learned readily.

Verification of lesions. The animal was sacrificed on April 12, 1937, 13 months after the first operation. The lesions (Fig. 3A) include the regions of the frontal lobe known to be essential for delayed reaction performance. The cortex corresponding to Brodmann's area 9-10-11-12 was completely ablated except for a few shreds of tissue on the extreme posterior surface of area 9.

Experiment 2.—Bilateral ablation of the frontal areas in two stages; retention of shuttle-box habit, abolition of delayed reaction, postoperative learning of temporal discrimination maze (Frontal 41).

The subject of this experiment was an immature female sooty mangabey (*Cercocebus torquatus atys*), weighing 2900 g. The animal had been observed for several months prior to training and was readily handled but remained excitable. Its *preoperative* training consisted of daily trials in the shuttle-box until the criterion of mastery was attained.

First operation—Ablation of left frontal areas (May 12, 1936). Under sodium amytal anesthesia, all tissue anterior to the inferior limb of the arcuate sulcus and its imaginary extension to the midline was removed. The weight of the freshly removed block was 2.6 g. *Recovery* was uncomplicated. By the first postoperative day appetite had returned and movements were executed normally, although activity was well marked. Neither reflex nor sensory impairment was detected and nothing in the animal's behavior after the third day suggested any abnormality.

Interoperative training (May 13–June 2, 1936). Daily test trials in the shuttle-box conducted during this interval showed that the preoperative level of performance was maintained.

Second operation (June 2, 1936). The right frontal areas were ablated following the

same procedure as before. The extirpated block weighed 2.2 g. *Recovery* was uneventful with no sensory or motor impairment. Hyperactivity and morbid hunger were first noticed on the fourth postoperative day and marked the entire postoperative course.

Postoperative training (June 3, 1936–Jan. 12, 1937). Testing on the shuttle-box was resumed on the first day and continued during the following three months, during which period it was shown that the habit had been retained. In the fifth postoperative month training on the delayed response was undertaken but the animal failed utterly to learn this problem. Training on the temporal discrimination maze was given seven months after operation and this habit was acquired efficiently. All work with this animal was interrupted shortly thereafter by the onset of sexual swelling and menstruation accompanied by marked behavioral changes.

Verification of lesions. The animal was sacrificed April 12, 1937, ten months after operation. Autopsy examination showed that the cortex anterior to the arcuate sulcus had been entirely destroyed in both hemispheres with the exception of a few mm. of tissue on the mesial surface which remained intact (Fig. 3B). This spared tissue, however, is posterior to the region essential to delayed reaction. Area 6 (premotor area) and the basal ganglia were undamaged.

Experiment 3—Simultaneous bilateral ablation of the frontal areas; retention of the temporal discrimination maze habit (Frontal 42).

The subject of this experiment, an immature female sooty mangabey (*Cercocebus torquatus atys*), weighing 2000 g. was exceptionally timid, but tractable and easily handled. *Preoperative* training was concerned exclusively with the temporal discrimination maze.

Operation—Ablation of frontal areas of both sides (Nov. 13, 1936). An attempt was made to remove in one piece, all tissue anterior to areas 6 and 8 in the left hemisphere. The extirpated block weighed 2.4 g. in the fresh state. A similar but slightly larger lesion (2.6 g.) involving the corresponding regions was made in the right hemisphere. On the second *postoperative* day some restriction of the conjugate movement of the eyes to the right was observed. There was no perceptible impairment of posture or locomotion. No hyperactivity was noted, although the appetite was apparently increased beginning the fourth day following operation. The wound healed by first intention.

Postoperative training (Nov. 15–Dec. 6, 1936). Beginning 2 days after operation, routine testing on the temporal discrimination maze was resumed which showed that the habit had been retained.

Verification of lesions. On the 30th day after operation, the animal died following a second operation involving the parietal areas. The extent of the lesions of the frontal areas made in the first operation is shown in Fig. 3C. (A second lesion in the parietal lobe also visible in the Fig. 3C is irrelevant to the present consideration.) All tissue anterior to the inferior limb of the arcuate sulcus excepting a few mm. immediately anterior, identified as area 8, had been removed. The posterior limits of the lesions were equivalent on the two sides and corresponded to the posterior boundary of Brodmann's area 9.

Experiment 4—Simultaneous bilateral ablation of frontal areas; retention of temporal discrimination maze habit, abolition of delayed response.

The subject of this experiment was an immature male mangabey (*Cercocebus torquatus atys*), weighing 4000 g. The animal was under observation for several months before experimentation, and proved cooperative and easily handled. Prior to operation the animal was trained in the temporal discrimination maze and in the delayed response apparatus.

Operation—Ablation of both frontal areas (Nov. 19, 1936). Under sodium amytal anesthesia, all tissue anterior to Brodmann's area 6, save the eye-fields, was removed from the left hemisphere in one block weighing 2.1 g. The corresponding regions on the right side were similarly removed, the block weighing 2.0 g. During *recovery* there were no sensory or motor disturbances, except for some restriction of ocular movement on the second day. The onset of pulmonary tuberculosis (verified at autopsy) at this time presumably accounted for the animal's loss of appetite and initiative.

Postoperative training (Nov. 21–Dec. 24, 1936). Testing on the temporal maze was instituted on the second day following operation and the animal maintained his previous level of mastery of this habit. During the period from the 15th to 34th days, testing on the delayed response problem was conducted but the ability to respond correctly of this test had not been retained.

Verification of lesions. The animal was sacrificed on the 56th postoperative day. The

approximate boundaries of the lesion are visible in Fig. 3D. In both hemispheres, all tissue identifiable as areas 9-10-11-12 had been removed save for 1 mm. of badly traumatized tissue on the lateral aspect of area 9. No injury had been caused to the basal ganglia; the ventricles had been spared, and area 6 appeared undamaged. The posterior limit of the lesion was well in back of the region shown by Jacobsen, Haslerud and Taylor to mediate delayed response.

REFERENCES

1. BARUK, H. *Les troubles mentaux dans les tumeurs cérébrales. Etude cliniques, pathogenie, traitement.* Paris: O. Doin, 1926. (Cited by Brickner.)
2. BIANCHI, L. *The mechanism of the brain and the function of the frontal lobes* (Transl. by J. H. MacDonald). Edinburgh: E. and S. Livingstone, 1922. 20, 348 pp.
3. BRICKNER, R. M. An interpretation of frontal lobe function based on a case of bilateral partial frontal lobectomy. *Res. Publ. Ass. nerv. ment. Dis.*, 1932, *13:* 259–351.
4. BRODMANN, K. *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellet auf Grund des Zellenbaues.* Leipzig: J. A. Barth, 1925, xii, 324 pp.
5. DUNLAP, K., GENTRY, E., and ZIEGLER, T. W. The behavior of white rats under food and electric shock stimulation. *J. comp. Psychol.*, 1931, *12:* 371–378.
6. ELDER, J. H., and NISSEN, H. W. Delayed alternation in raccoons. *J. comp. Psychol.*, 1933, *16:* 117–135.
7. FERRIER, D. *The functions of the brain.* London: Smith, Elder and Co., 1876. xv, 323 pp.
8. FRANZ, S. I. On the functions of the cerebrum: the frontal lobes. *Arch. Psychol.*, 1907, *1:* 1–64.
9. FULTON, J. F., and JACOBSEN, C. F. The functions of the frontal lobes, a comparative study in monkeys, chimpanzees and man. *Advances Modern Biol.*, 1935, *4:* 113–123.
10. FULTON, J. F., and KELLER, A. D. *The sign of Babinski. A study of the evolution of cortical dominance in primates.* Springfield, Illinois: Charles C Thomas, 1932. xi, 165 pp.
11. GENTRY, E. Methods of discrimination training in white rats. *J. comp. Psychol.*, 1934, *18:* 227–258.
12. GOLDSTEIN, K. The significance of the frontal lobes for mental performances. *J. Neurol. Psychopath.*, 1936, *17:* 27–40.
13. HARLOW, H. F. The neuro-physiological correlates of learning and intelligence. *Psychol. Bull.*, 1936, *33:* 479–525.
14. HILGARD, E. R. Conditioned eyelid reactions to a light stimulus based on the reflex wink to sound. *Psychol. Monogr.*, 1931, *41:* 50 pp.
15. HULL, C. L. A functional interpretation of the conditioned reflex. *Psychol. Rev.*, 1929, *36:* 498–511.
16. JACKSON, J. HUGHLINGS. *Selected Writings, Vol. II.* London: Hodder and Stoughton, Ltd., 1932. vii, 510 pp.
17. JACOBSEN, C. F. Recent experiments on the functions of the frontal lobes. *Psychol. Bull.*, 1928, *25:* 1–11.
18. JACOBSEN, C. F. A study of cerebral function in learning. The frontal lobes. *J. comp. Neurol.*, 1931, *52:* 271–340.
19. JACOBSEN, C. F. Functions of the frontal association area in primates. *Arch .Neurol. Psychiat., Chicago*, 1935, *33:* 558–569.
20. JACOBSEN, C. F. Studies of cerebral function in primates. I. The functions of the frontal association areas in monkeys. *Comp. Psychol. Monogr.*, 1936, *13:* 1–60.
21. JACOBSEN, C. F., and ELDER, J. H. Studies of cerebral function in primates. II. The effect of temporal lobe lesions on delayed response in monkeys. *Comp. Psychol. Monogr.*, 1936, *13:* 61–65.
22. JACOBSEN, C. F., and HASLERUD, G. M. Studies of cerebral function in primates. III. A note on the effect of motor and premotor area lesions on delayed response in monkeys. *Comp. Psychol. Monogr.*, 1936, *13:* 66–68.
23. JACOBSEN, C. F., HASLERUD, G. M., and TAYLOR, F. V. Personal communication.
24. JACOBSEN, C. F., and NISSEN, H. W. Studies of cerebral function in primates. IV. The effects of frontal lobe lesions on the delayed alternation habit in monkeys. *J. comp. Psychol.*, 1937, *23:* 101–112.

25. JACOBSEN, C. F., WOLFE, J. B., and JACKSON, T. A. An experimental analysis of the functions of the frontal association areas in primates. *J. nerv. ment. Dis.*, 1935, *82:* 1–14.
26. KÖHLER, W. *The mentality of apes*, New York: Harcourt, Brace and Co., 1926. viii, 336 pp.
27. KRECHEVSKY, I. Brain mechanisms and hypotheses. *J. comp. Psychol.*, 1935, *19:* 425–468.
28. LASHLEY, K. S. *Brain mechanisms and intelligence.* Chicago: Univ. Chicago Press, 1929. xiv, 186 pp.
29. LASHLEY, K. S. Studies of cerebral function in learning. XI. The behavior of the rat in latch box situations. *Comp. Psychol. Monogr.*, 1935, *11:* 1–43.
30. LASHLEY, K. S. Learning III. Nervous mechanisms in learning. Chapter 10 in Murchison. *A handbook of general experimental psychology.* Worcester, Mass., Clark University Press, 1934 (pp. 456–496).
31. LEPLEY, W. M. A theory of serial learning and forgetting based upon conditioned reflex principles. *Psychol. Rev.*, 1932, *39:* 279–288.
32. LOUCKS, R. B. Efficacy of the rat's motor cortex in delayed alternation. *J. comp. Neurol.*, 1931, *53:* 511–567.
33. MAIER, N. R. F. The effect of cerebral destruction on reasoning and learning in rats. *J. comp. Neurol.*, 1932, *54:* 45–75.
35. MAIER, N. R. F. Cortical destruction in the posterior part of the brain and its effect on reasoning in rats. *J. comp. Neurol.*, 1932, *56:* 179–214.
36. MESSIMY, R. Les effets, chez le singe, de l'ablation des lobes préfrontaux. *Rev. neurol.*, 1939, *71:* 1–37.
37. MESSIMY, R., and FINAN, J. Les effets, chez le singe, de l'ablation des lobes préfrontaux. Modifications de l'activité et du mode réactionnel. *C. R. Soc. Biol., Paris*, 1937, *126:* 201–203; see also Les effets, chez le singe, de l'ablation des lobes préfrontaux. Modifications des réflexes notamment des réflexes de posture. Modification du système autonome. *C. R. Soc. Biol., Paris*, 1937, *126:* 203–206.
38. PENFIELD, W., and EVANS, J. Functional defects produced by cerebral lobectomies. *Res. Publ. Ass. Res. nerv. ment. Dis.*, 1934, *13:* 352–377.
39. RUCH, F. L. L'appreciation du temps chez le rat blanc. *Année psychol.*, 1931, *32:* 118–130.
40. SAMS, C. F., and TOLMAN, E. C. Time discrimination in white rats. *J. comp. Psychol.*, 1925, *5:* 255–264.
41. SWITZER, S. A. Anticipatory and inhibitory characteristics of delayed conditioned reactions. *J. exp. Psychol.*, 1934, *17:* 603–620.
42. TOLMAN, E. C. Theories of learning in comparative psychology. Chapter 12 in Moss. *Comparative psychology.* New York: Prentice-Hall, Inc., 1934, pp. 367–408.
43. WENDT, G. R. An interpretation of inhibition of conditioned reflexes as competition between reaction systems. *Psychol. Rev.*, 1936, *43:* 258–281.
44. WOODROW, H. Discrimination by the monkey of temporal sequences of varying numbers of stimuli. *J. comp. Psychol.*, 1929, *9:* 123–158.
45. WOODROW, H. Temporal discrimination in the monkey. *J. comp. Psychol.*, 1929, *8:* 395–427.

RELATION OF STIMULATION TIME OF RECEPTORS TO RECOVERY TIME IN THE NERVOUS SYSTEM: VISUAL, OLFACTORY AND AUDITORY SENSES*

CHARLES A. ELSBERG AND H. SPOTNITZ
Clinical Research Laboratories of the Neurological Institute of New York

(Received for publication February 10, 1939)

IN OUR studies of the special senses of vision, smell and hearing, investigations were made of the relationship between the time of action of a specific stimulus, and the time required for recovery from the stimulus. The results of these investigations appear to demonstrate that there is a simple mathematical relationship between stimulation time and recovery time. While the peripheral receptors must play an important part,—photochemical in vision, physical or physicochemical in smell and hearing,—the speed of recovery (*i.e.*, of the return to equilibrium) appears to be based upon a neural factor common to all of the special senses that were investigated.

The principles on which the tests of olfaction and of vision are based, and the apparatus used and procedures followed, have been described in detail in papers published previously. For the tests of vision, the minimum intensity of light required to see a test object was first ascertained. The eye or eyes were then exposed for increasing lengths of time to a brighter light of known intensity. The time required after each light adaptation, until the individual could again recognize the test object illuminated by threshold light, was the time required for recovery (*i.e.*, the time required for dark adaptation).

For the olfactory tests, the minimum volume of odor required for the recognition of an odorous substance was first ascertained. The olfactory membrane was then exposed for increasing lengths of time to a stream of air and odor of a definite volume-rate, and in each test the time required until the individual could again recognize the odor at its threshold value (the minimum identifiable odor, or MIO) was the time required for recovery from olfactory fatigue (olfactory adaptation). The apparatus used and the methods for testing hearing will be described in detail in another report. They are based on a similar principle to that on which the olfactory and visual tests are based. For our present purpose, the following facts may be mentioned. The apparatus used was the audiometer 6A made by the Western Electric Company, by which the wave frequency can be varied up to 8190, and the intensity can be varied between 0 and 120 decibels. The sound was conveyed to the ears by double ear-phones which were allowed to remain in place during each series of tests—no matter whether one or both ears were stimulated.

The threshold for a tone of any frequency was first ascertained. The threshold was the minimum intensity which could be recognized when one or both ears were exposed to the tone for periods of one second at intervals of one second. The ear was then exposed to a greater intensity of the same tone† for increasing lengths of time, and then to the threshold intensity which had previously been determined, until the tone was recognized. In each test, the time that elapsed from the conclusion of the more intense stimulation to the time when the threshold stimulus was again recognized was the period required for recovery (the duration of auditory fatigue or the time required for auditory adaptation).

TESTS OF THE VISUAL SENSE

A large number of tests of foveal vision with red light (beyond 610$\mu\mu$ of the spectrum) showed that there is a simple mathematical relation between

* Work done under a grant from the John and Mary R. Markle Foundation.

† With the apparatus at present available, it is impossible to reproduce exactly the same tone at a higher as at the lower intensity (see Stevens and Davis, 1938, pp. 72–73). The differences are, however, so small that they may be disregarded.

the time during which the eye was exposed to the light stimulus (light adaptation) and the time required for dark adaptation (*i.e.*, the time which elapsed before a threshold stimulus could again be recognized as such). It was found that for each intensity of light the square root of the recovery time divided by the cube root of stimulation time had a constant value, or

$$\frac{\sqrt{\text{Recovery Time}}}{\sqrt[3]{\text{Stimulating Time}}} = C, \text{ or } \frac{RT^{1/2}}{StT^{1/3}} = C, \text{ or } \frac{RT}{StT^{2/3}} = C.$$

This relationship between stimulation time and recovery time is shown, for example, by the following series of tests for light intensities of 40 and 80 foot candles (at a distance of 40.5 cm. from the eyes).

Table 1. Test object with contrast. Total area 6400 sq. mm.; white area 1600 sq. mm., black area 4800 sq. mm. Intensity of illumination of test object 5.4 foot candles at a distance of 3.75 m. Intensity of bright light used for light adaptation 40 foot candles. Duration of exposure to bright light 5, 10, 15, 20, 25 and 30 sec. Averages of 3–5 tests.

Time of Stimulation	Time of Dark Adaptation	Time of Stimulation$^{2/3}$	Time of Dark Adaptation ÷ Stimulation Time$^{2/3}$	Calculated Time of Dark Adaptation	
				Based on $C = 2.63$	Based on average of $C = 2.67$
sec.	sec.			sec.	sec.
5	7.9	2.92	2.63	7.7	7.8
10	11.9	4.64	2.56	12.2	12.4
15	16.1	6.1	2.64	16.04	16.3
20	19.9	7.4	2.68	19.5	19.8
25	22.6	8.6	2.63	22.6	23.0
30	24.7	9.7	2.55	25.5	25.9

Table 2. Test object with contrast. Total area 6400 sq. mm. Intensity of illumination of test object 4.96 foot candles; intensity of light used for light adaptation 80 foot candles. Duration of exposure to bright light 30, 60, 90 and 120 sec. Average of 3–4 tests.

Time of Stimulation	Time of Dark Adaptation	Stimulation Time$^{2/3}$	Time of Dark Adaptation ÷ Stimulation Time$^{2/3}$	Calculated Time of Dark Adaptation Based on Average of $C = 29.9$
sec.	sec.			sec.
30	27.5	9.7	2.83	29.
60	47.6	15.4	3.09	46.04
90	60.4	20.0	3.02	59.8
120	77.7	24.5	3.02	73.3

Tests of the Olfactory Sense

From the following illustrative tests, it is demonstrated that for the sense of smell, the relation between stimulation time and recovery time for odor used, is the same as that for vision, namely,

$$\frac{RT}{StT^{2/3}} = C$$

Table 3. Coffee odor; unilateral tests of right nasal passage; MIO 8; stream injection of odor 2000 cc. per min.

Duration of Stream Injection	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 12.9
sec.		sec.		sec.
10	4.64	60	12.9	59.9
20	7.4	90	12.2	95.5
30	9.7	120	12.4	125.1
60	15.4	210	13.6	198.6

Table 4. Coffee odor; unilateral tests of right nasal passage; MIO 8; stream injection of odor 4000 cc. per min.

Duration of Stream Injection	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 30.8
sec.		sec.		sec.
5	2.92	90	30.8	89.9
15	6.1	180	29.5	187.9
25	8.7	270	31.0	267.9

Table 5. Citral odor; unilateral tests of right nasal passage; MIO 7; stream injections of odor 2000 cc. per min.

Duration of Stream Injection	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 28.3
sec.		sec.		sec.
10	4.64	120	25.8	120.0
20	7.4	210	28.3	190.9
30	9.7	270	27.8	250.3

Table 6. Citral odor; unilateral test of right nasal passage; MIO 8; stream injections of odor 1000 cc. per min.

Duration of Stream Injection	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 11.0
sec.		sec.		sec.
20	7.4	60	8.11	81.4
30	9.7	120	12.3	106.7
60	15.4	180	11.7	169.4
120	24.5	270	11.0	269.5

Tests of the Auditory Sense

As shown by the series of tests in Tables 7, 8 and 9, the relation between stimulation time and recovery time for the auditory sense was the same as that for the visual and olfactory senses, namely

$$\frac{RT}{StT^{2/3}} = C$$

for each frequency used in the tests.

Table 7. Binaural tests at threshold; intensity of stimulation 92 decibels. Frequency 1024. Tests at 15-second intervals. Averages of 3 to 5 tests.

Stimulation Time Injection	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 1.2
sec.		sec.		sec.
5	2.92	4	1.36	4.50
10	4.64	5	1.19	5.6
15	6.1	7.5	1.23	7.3
20	7.4	9.1	1.23	8.9
30	9.7	11.9	1.21	11.6

Table 8. Left ear tested at threshold; intensity of stimulation 90 decibels. Frequency 1024. Tests at 15-second intervals. Averages of 3 to 5 tests.

Stimulation Time	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 1.74
sec.		sec.		sec.
5	2.92	5.1	1.74	5.8
10	4.64	8.2	1.76	8.1
15	6.1	10.8	1.76	10.6
20	7.4	12.5	1.70	12.9
30	9.7	18.0	1.84	16.9

Table 9. Left ear tested at threshold; intensity of stimulation 80 decibels. Frequency 2048. Tests at 15-second intervals. Averages of 3 to 5 tests.

Stimulation Time	Stimulation Time$^{2/3}$	Recovery Time	Recovery Time ÷ Stimulation Time$^{2/3}$	Recovery Time Calculated on Basis of 2.7
sec.		sec.		sec.
5	2.92	7.9	2.7	7.9
10	4.64	12.0	2.58	12.5
15	6.1	16.2	2.65	16.5
20	7.4	18.4	2.49	19.9
30	9.7	25.2	2.6	26.2

Discussion

It is well known that excessive stimulation of a peripheral receptor can lead to alterations in the structure and function of that receptor, which may take many hours for complete recovery. In our investigations of recovery time only moderate stimuli were utilized. These were based upon the principle clearly expressed by Froehlich that the central nervous system fatigues for comparatively weak stimuli according to the principles of relative fatigue. It was found that the difference in intensity between the fatiguing stimulus and the threshold stimulus determined the maximum recovery time. As the difference between the two intensities increased, the recovery time was lengthened; as the difference decreased, the recovery time became shortened. Thus the limits within which the stimulation time formula held was determined in part by the difference in intensity between the moderate stimulus and the threshold stimulus.

There were two other limiting factors for the recovery time formula: (i) the effect of stimulation time was limited. For the sense of smell it was observed that the recovery period was not lengthened when the stimulation time was longer than 3 min. For the senses of vision and hearing there was usually no significant increase in the recovery time when the stimulation time was longer than one and one-half minutes. (ii) Under normal conditions, the maximum duration of the recovery period of the sense of smell was usually about 7–9 minutes; for the sense of vision, the maximum recovery period was about 80 sec., and for the sense of hearing about 40 sec.

The formula: Stimulation Time$^{2/3}$ ÷ Recovery Time = Constant enabled one to predict the recovery time only when the duration of the stimulation time was less than the maximum effective stimulation time and only when the duration of the recovery time was less than the maximum recovery time obtainable with the stimulus.

In our investigations of the literature we have been unable to find any studies concerning the quantitative relation between stimulation time and recovery time in which the *intensity* of stimulation was kept constant but the *time* of stimulation was varied. The fact that recovery time was proportional to the $\frac{2}{3}$ power of the stimulation time was referred to in a paper by one of the writers (Mills Memorial Lecture). In that paper we recorded the fact that a large series of tests of foveal vision with red light showed that, if the test object and the intensity of light by which it is illuminated are kept constant, the formula for dark adaptation could be expressed as:

$$TDA \div (I^{1/3} \times StT)^{2/3} = C^*.$$

From this equation it was possible to suspect that if the intensity of the stimulating light was kept the same *i.e.*, if in the above equation I is a constant and is given any value (say 1) then

$$TDA \div StT^{2/3} = C$$

* TDA = Time required for Dark Adaptation; I = Intensity of light used for light adaptation; St T = Stimulation Time; C = Constant.

or the time required for dark adaptation (time of recovery) divided by the $\frac{2}{3}$ power of the time of stimulation should have a constant value. In other words, the recovery time should be proportional to the $\frac{2}{3}$ power of the stimulation time. In the tests described in this report, the visual experiments were actually made with a constant intensity of stimulation and the relationship between stimulating time and recovery time was found to be that which had been predicated from our previous tests.

That the same simple mathematical relationship between stimulating time and recovery time was also found in tests of the olfactory and the auditory senses appears to indicate that this relationship may be a general one. In the present state of knowledge, such a generalization may be only suspected until the time when based on the same principle, quantitative tests of the sense of taste and of the various modalities of somatic sensation have been carried out or have become possible. In the tests of the visual sense, the relationship between stimulating time and recovery time held only when the entire peripheral receptor (retina) was stimulated. If the experiments were so arranged that only one-half of the retina was stimulated by the bright light (*i.e.*, was light adapted), then the relationship was altered.

In a previous report, we have made the suggestion that this $\frac{2}{3}$ power might indicate that the recovery time depends upon a surface reaction. The evidence which appears to make it probable that this surface reaction occurs in the nervous system and not in the peripheral receptor apparatus has been summarized in a paper already published. There were some indications in our tests that a changed mathematical relation between the reaction of the peripheral receptors and the reaction of the nervous system may result under special conditions. As yet the significance of these alterations is not at all clear.

The mathematical relationship between stimulation time and recovery time suggested in this report, is in all probability only an approximation, but by means of this relationship it has been possible usually to predict (within the error of the experiments) the results of other tests from one experiment.

Summary

1. For the special senses of vision, smell and hearing, there is the same simple mathematical relationship between the duration of stimulation of the peripheral receptors and the duration of the recovery period.

2. This relationship indicates that the duration of the recovery period is proportional to the $\frac{2}{3}$ power of the duration of stimulation.

3. This relationship is limited by certain factors.

4. The relationship may be based upon a neural factor common to all of the senses that were investigated.

REFERENCES

ELSBERG, C. A. The Charles K. Mills Memorial Lecture. Cerebral activity including conscious sensation as a physicochemical process with evidence to indicate that many vital processes can be expressed in simple mathematical relationships. *Bull. neurol. Inst. N. Y.*, 1938, *7:* 212–244.

ELSBERG, C. A., and LEVY, I. A new and simple method of quantitative olfactometry. *Bull. neurol. Inst. N.Y.*, 1935, *4:* 5–19.

ELSBERG, C. A., and SPOTNITZ, H. A method for the study of acuity of vision and of relative visual fatigue. *Bull. neurol. Inst. N.Y.*, 1937, *6:* 234–242.

ELSBERG, C. A., and SPOTNITZ, H. The relative refractory period of olfaction and vision. *Bull. neurol. Inst. N.Y.*, 1938, *7:* 78–94.

ELSBERG, C. A., and SPOTNITZ, H. Is cerebral activity a physicochemical process: studies based on the physicochemical equivalents of a formula for dark adaptation. *J. gen. Psychol.*, 1938, *19:* 263–276.

FROEHLICH, F. W. Beiträge zur Analyse der Reflexfunktion des Rückenmarks. *Z. allg. Physiol.*, 1908, *9:* 55.

FROEHLICH, F. W. Experimentelle Studien am Nervensystem der Mollusken. *Z. allg. Physiol.*, 1919, *11:* 275.

FROEHLICH, F. W. Über die rhythmische Natur der Lebensvergänge Sammelreferat *Z. allg. Physiol.*, 1912, *13:* 1.

FROEHLICH, F. W. Beiträge zur allgemeinen Physiologie der Sinnesorgane. *Z. Psychol. Physiol. Sinnesorg.*, 1913, *48:* 28, 165, 354.

STEVENS, S. S., and DAVIS, H. *Hearing—Its psychology and physiology*. New York: John Wiley & Sons, 1938, xvi, 490 pp.

ANATOMY, PHYSIOLOGY AND SURGICAL CONSIDERATIONS OF THE SPINAL TRACT OF THE TRIGEMINAL NERVE*

A. EARL WALKER
From the Division of Neurology and Neurosurgery, University of Chicago Clinics

(Received for publication February 11, 1939)

INTRODUCTION

A PRIME essential for the success of surgical intervention to relieve trigeminal pain is a knowledge of the finer anatomical and physiological relationships of the fifth cranial nerve. Neurosurgeons, realizing this fact, have in large measure been responsible for the careful experimental, clinical and anatomical studies of the fiber arrangement of the trigeminal root. Recently, for the relief of facial pain, several operative procedures on the central trigeminal pathways[7,15] have been suggested, the most promising being section of its descending tract[16]. A study of the anatomy and physiology of the spinal tract of the trigeminal nerve then becomes increasingly pertinent.

Central terminations of the fifth nerve

Although embryologically the fifth cranial nerve is homologous to a spinal nerve, its central relationships are quite different. In the human embryo His[12] noted that the "root pieces" of the trigeminal nerve arise out of bundles with a crossed course. Windle[23] has confirmed this observation in the cat embryo in which the fibers from the anteriorly developing ophthalmic division of the ganglion enter posteriorly and somewhat medial to those from the mandibular and maxillary divisions. With further development and curvature of the brain stem, the entrance zone of the ophthalmic division comes to lie in the inferior and medial portion of the root. In support of this theory Davis and Haven[6] state that in cats partial section of the root, as practiced in human beings, produces a keratitis, and anaesthesia of the forehead and maxilla.

This arrangement of the root of the fifth nerve has been questioned by Sjöqvist[16] on the basis of his fiber analysis. He found that the fibers with a diameter of 4μ or less, to which presumably belong those conveying pain and temperature, are more numerous in the ophthalmic division of the trigeminal nerve and in the upper part of the sensory root throughout its extent. He concluded, therefore, that there was no rotation of the root to such a high degree as supposed by Windle[23] and Davis and Haven.[6] He did not find the small fibers arranged peripherally as did Windle in the cat or cen-

* Presented, in part, before the Chicago Society of Internal Medicine, February 27, 1939.

trally as Davis and Haven[6] found in man. While Davis and Haven[6] state that the portion cut in Dandy's suboccipital operation on the trigeminal root is the ophthalmic division, Sjöqvist[16] maintains that it is the maxillo-mandibular group, and states that the sensory changes present are found about the mouth or lower lip. Although Dandy[5] does not admit consistent sensory alterations following this operation, most writers support Sjöqvist's contention. In Bailey's experience[1] the perioral region shows sensory changes. In two such cases Van Wagenen[19] found disturbances in sensation around the mouth.

The arrangement of the fibers passing into the pons has been studied in the newborn mouse by Cajal.[4] The majority bifurcate, one branch passing superiorly and one down the tract of the spinal root of the trigeminal nerve. Cajal,[4] however, stated that he could not be sure that all fibers bifurcated. Later investigators have laid little stress on the non-bifurcating fibers, although the majority admit their presence. In 1923 Gerard[10] studied the entering fibers of the fifth nerve on pyridine silver preparations of the cat's brain. She believed that the majority divided, but admitted that she saw no bifurcation of small fibers, either myelinated or unmyelinated. Windle[22] studied the brain stems of newborn mice and foetal pigs impregnated by Golgi silver method. He describes three types of fibers: (i) Heavy fibers which divide dichotomously in a typical T or Y shape, one branch ascending to the main sensory nucleus and the other going inferiorly to the spinal nucleus of the fifth nerve. (ii) Some fine fibers bifurcate, but the majority turn downward at the peripheral margin of the bifurcating fibers to pass into the spinal root of the trigeminal nerve without branching. (iii) A few fibers, usually of large size, turn upward to enter the main sensory nucleus without giving off a descending branch. The following were the proportions of these fibers:

Bifurcating fibers	51.34 per cent
Descending non-bifurcating	42.25 per cent
Ascending non-bifurcating	6.41 per cent

The topical arrangement of the fibers in the spinal tract of the fifth nerve seems to be fairly well agreed upon by all investigators. Bergman[2] showed that when the sensory root was completely degenerated at its entrance into the pons, the spinal tract was likewise fully degenerated. After experimental lesions of the root, Bergman[2] noted that those animals having an absent corneal reflex and marked keratitis had degeneration in the ventral part of the spinal tract. When the corneal reflex was preserved and the keratitis absent only the dorsal portion of the tract was degenerated. In 1901 Spiller and Frazier[18] confirmed this localization and in 1904 Wallenberg,[21] and in 1907 Kutner and Kramer[13] independently, came to the same conclusion. The last believed, however, that the ophthalmic division extended to the lowest level in the spinal tract of the fifth nerve, the maxillary

fibers did not reach so far and the mandibular fibers passed down a still shorter distance.

The significance of this arrangement of the fibers of the spinal tract of the trigeminal nerve has been indicated by several previous writers. Both Winkler[24] and Spiller[17] have suggested that the fibers which pass down the spinal tract are concerned in the appreciation of pain and temperature, while those which terminate in the main sensory nucleus are carrying touch and proprioception. Later writers have confirmed this finding on both clinical and experimental grounds. Gerard[10] concluded from an analysis of clinical cases of thrombosis of the posterior inferior cerebellar artery that the impulses carrying pain and thermal sensibilities from the fifth nerve descend through the bulb in the spinal tract of that nerve, and pass at various levels to the cells of the spinal nucleus; whereas the tactile impulses from the face pass to the cells of the main sensory nucleus. Her studies following experimental section of the spinal trigeminal root in the bulb of the cat pointed to the same conclusion.

Sjöqvist[16] in a recent study of pain conduction in the trigeminal nerve has utilized the findings of Gasser and Erlanger[8] that finely myelinated fibers carried pain and temperature sensibilities. Sjöqvist's[15] analysis (expressed as percentage of total fibers) of the fibers of the spinal tract of the macaque monkey which he stated was similar to that of man, is as follows:

	Less than 3μ	Less than 4μ
Level of the superior olive	71.8	85.0
Just above inferior olive	77.0	89.4
Caudal part of the inferior olive	80.9	91.9

Because this tract contains such a large percentage of small fibers he concludes that it must be concerned with the passage of pain and thermal impulses. However, in an apparently similar analysis carried out by Gerard*[10] (on the cat, but said to be comparable to man) there was a quite different ratio of small and large fibers in the spinal tract of the trigeminal nerve.

	Less than 3.7μ	Less than 4.8μ
Level of the superior olive	53.5	72.2
Just above inferior olive	48.2	74.6
Caudal part of the inferior olive	39.5**	69.6**

Moreover, although she states that the large fibers decrease in the lower levels of the trigeminal tract, her figures do not show that the relative proportion of smaller fibers is increased.

* The statistics given here are based on the average of the figures given by Gerard for 3 or 4 cases. The figures for the individual cases, however, did not vary greatly.

** This figure is probably slightly too small, because Gerard does not give the number of myelinated fibers measuring 0–3.7 μ at the lower level of the inferior olive. The calculations are based upon her figure for the fibers of this size at the bifurcation of the pyramids.

One must therefore conclude that although there is a large proportion of small fibers in the descending tract of the trigeminal nerve there are also larger fibers, whose size is comparable with that of the fibers known to carry touch and proprioception.

Clinical significance. The role of the spinal tract of the trigeminal nerve has been determined largely by clinical studies of dysfunction resulting from vascular lesions of the lateral portion of the medulla oblongata which is irrigated by the posterior inferior cerebellar artery. Thrombosis of this vessel produces a characteristic syndrome, one element of which is usually said to be a dissociated anaesthesia on the ipsilateral side of the face. This is considered, and probably correctly so, the result of involvement of the spinal root of the trigeminal nerve. Practically all authors state that after this type of vascular insult there is a marked analgesia on the ipsilateral side of the face with preservation of tactile sensibility.

Observations

Two typical cases of this syndrome, both of the left posterior inferior cerebellar artery, have been carefully examined for the sensory changes on the face, neck and throat. Both cases had a left Horner's syndrome, sensory disturbances over the left side of the face, no masseter, pterygoid or facial weakness on either side, a hemihypalgesia on the right side below the face and incoordination of the left arm and leg. Both were examined at least one month after the ictus at which time they appeared to be reliable witnesses.

Method of examination. All examinations were carried out with the eyes closed or the patient blindfolded. Using Von Frey's hairs and pins, representative areas about 4 sq. cm. in size were stimulated at irregular times with one test object for ten times. The sequence was interrupted two or three times to stimulate some other area of the face to be certain that the attention was maintained. The series of ten stimulations usually took about one minute. A short rest was allowed between series, and if the patient showed any signs of fatigue, which readily manifested themselves by inconstant replies and inattention, the examination was terminated, and continued another day. The results are given as the number of stimuli correctly appreciated in a series of ten tests. On the whole the results obtained by these graduated series of stimuli were quite consistent.

Case 1. (HBF). The following were the results of graded stimulation of the face.

Pain	Forehead		Cheek		Chin	
Grams	R.	L.	R.	L.	R.	L.
0.125	0	0	0	0	0	0
0.5	0	0	0	0	0	0
0.75	6	0	5	0	0	0
1.0	6	1	3	0	7	0
2.0	8	0	9	0	6	0
4.0	10	2	10	3	10	0
6.0		0		0		0
8.0		0		0		0

If, however, the stimuli were rapidly repeated near the same point the patient complained bitterly of the pain, which was rather diffusely localized to the point stimulated. The pain of such stimulation was much more severe on the affected side than on the normal

Touch	Forehead		Cheek		Chin	
G./mm.	R.	L.	R.	L.	R.	L.
0.5	1	0	2	0	2	0
1.0	7	1	5	1	3	4
2.0	8	0	7	3	7	3
3.0	7	1	10	2	7	3
4.0	9	1	10	6	10	8
5.0	7	6	10	3	9	9
7.5	7	7	10	7	9	9
10.0	10	7	10	10	10	10
15.0		10				

CASE 2. (HH). Examination six months after thrombosis of the left posterior inferior cerebellar artery.

Touch	Forehead		Cheek		Chin	
G./mm.	R.	L.	R.	L.	R.	L.
0.5	1	0	7	0	3	0
1.0	7	0	6	0	7	0
2.0	9	0	9	1	9	2
3.0	10	0	10	3	10	4
4.0	10	0	10	3	10	4
5.0	10	2	10	4	10	4
7.5	10	4	10	5	10	6
10.0	10	5	10	7	10	7
15.0	10	8	10	10	10	10
Pain						
Gm.						
0.125	0	0	0	0	0	0
0.5	3	0	3	0	1	0
0.75	9	0	9	0	9	0
1.0	10	0	10	0	10	0
2.0		0		0		0
4.0		0		1		1
6.0		1		3		2
8.0		1		2		2

Heat and cold are lost in the same distribution on the face as pin prick. The tongue, soft palate and pharynx on the left side are analgesic. The patient says that he has a constant burning pain in the left side of the face.

Comment. These cases lack the conclusiveness afforded by anatomical verification of the lesion. The clinical findings would suggest, however, that the softenings were largely confined to the medulla oblongata, and did not involve pontine structures; for there was no weakness of the facial, masseter, pterygoid or external rectus muscles. It seems likely, then, that the main sensory nucleus of the fifth nerve was not involved by the softening. One may, therefore, assume that the sensory disturbances in the face were due to interruption of the descending tract of the fifth nerve. It then follows that the latter carries fibers which are mainly, but not exclusively, concerned

in the transmission of pain and temperature sensibilities. Tactile impulses are also carried in this tract.

Trigeminal tractotomy

The recently devised operation of trigeminal tractotomy offers an opportunity to study the sensory defects following a lesion practically confined to the descending root of the fifth nerve. In this operation the spinal tract of the trigeminal nerve is sectioned with a sharp scalpel at the level of the middle of the inferior olive (Fig. 1).

FIG. 1. Section through the bulb at approximately the middle of the inferior olivary nucleus to show the position of the descending root of the trigeminal nerve and (cross-hatched) the extent of the incision in the operation of trigeminal tractotomy. (Kulschitsky myelin stain ×6.)

Sjöqvist[16], who devised the operation, suggested it as an alternative to section of the trigeminal root in the posterior fossa. Such a procedure might have certain advantages over the classical retrogasserian neurectomy. (1) Since touch is largely preserved the disagreeable numbness which frequently follows retrogasserian neurectomy might be avoided (2). Keratitis might be less likely to develop (3). It could be performed in an individual in whom the temporal route was inadvisable owing to local neoplastic in-

volvement or infection (4). Facial and masseter paralysis could be more easily avoided. Whether all these advantages will be realized remains to be determined for as yet only 11 cases* have been reported, 9 by Sjöqvist[16] and 2 in this paper. That dysesthesias will be eliminated by this procedure seems unlikely in view of the fact that patients with posterior inferior cere-

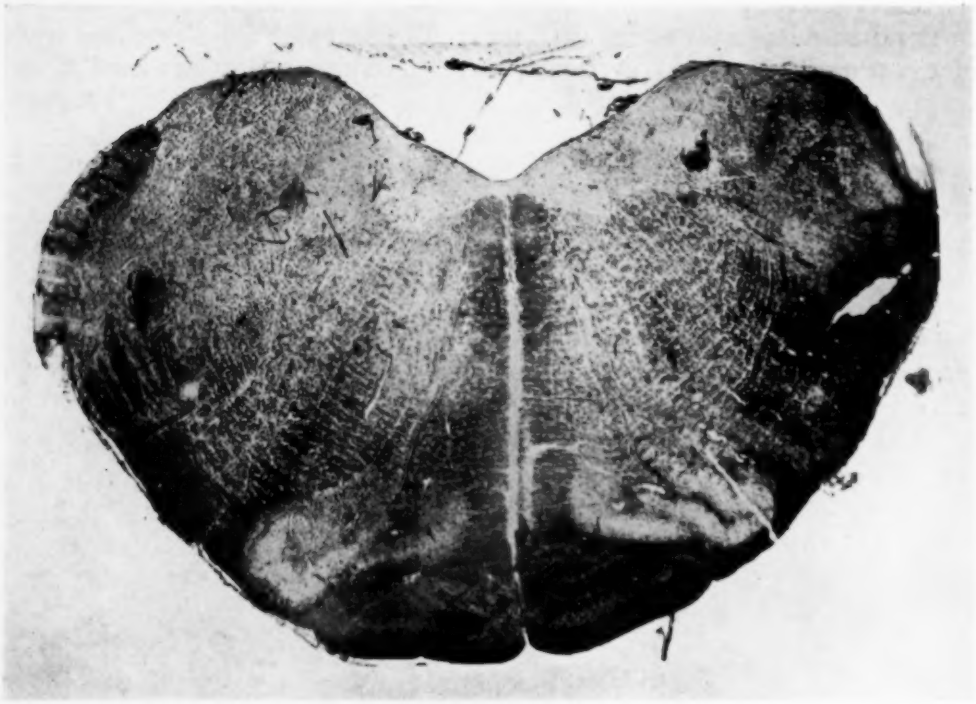

FIG. 2. Section through the bulb at the level of the inferior third of the inferior olivary nucleus to show the actual section of the descending root of the trigeminal root in the macaque monkey. (Marchi preparation ×6.) (M-4-38, Bl. viii, 2.)

bellar thrombosis frequently complain of a burning pain in the ipsilateral side of the face.

But there are certain obvious disadvantages to this operation. (i) The operative field is in the posterior fossa, where bleeding is frequently difficult to control without grave consequences, and from whence one cannot retreat so readily as from the middle fossa. (ii) It is difficult to be sure that enough of the tract has been cut. In two of Sjöqvist's patients no sensory disturbances could be demonstrated postoperatively, and in one of the present cases the first division fibers were spared, rendering the operation only

* Since writing this paper Rowbotham (ROWBOTHAM, G. F.: Treatment of pain in the face by intramedullary tractotomy. *Brit. med. J.* 1938, *2:* 1073–1076) has reported 3 additional successful cases, and Jackson and Ironsides (JACKSON H., and IRONSIDES, R. Left trigeminal pain treated by Sjöqvist's medullary trigeminal tractotomy. *Proc. R. Soc. Med.* (Sect. Neurol.), 1938, *32:* 219–220) have added a further case.

partially successful. (iii) In three of Sjöqvist's cases involvement of the vagus root gave unilateral laryngeal paralysis. Although temporary in one case, the voice remained husky in other cases. (iv) Although no fatalities are reported to date, I doubt that the operation if used routinely, even in the hands of the most experienced neurosurgeons, would carry as low a mortality as the classical retrogasserian neurectomy.

For this reason the operation is not suggested as a routine procedure, but only to be used in carefully selected cases. It should be particularly valuable for the relief of pain in the neck and face from neoplastic lesions. In these cases it is frequently desirable to section the upper dorsal posterior roots as well as the sensory fibers from the face. Tractotomy in these cases is a much simpler procedure than section of the trigeminal root as it enters the pons.

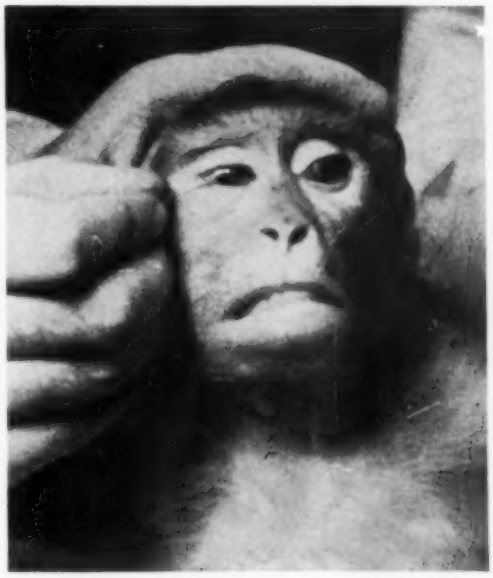

FIG. 3. Photograph of a macaque monkey (M-4-38) to show the results of section of the descending root of the trigeminal nerve. The absence of the corneal reflex and Horner's syndrome on the right side are apparent. The lesion in this case is shown in Fig. 2. (Exposure in this and the following illustration was 0.5 sec.)

Results of trigeminal tractomy. The operation was first tried on three macaque monkeys (Fig. 2). Immediately after operation the corneal reflex was constantly abolished and the animal did not respond to pin prick over the ipsilateral side of the face, although it did react to tickling of the ipsilateral nares. There was no weakness of the masseter muscles. In one animal there was a mild Horner's syndrome on the ipsilateral side (Fig. 3). The animals ran, jumped and climbed the day following operation without the slightest unsteadiness or abnormality in their gait. Encouraged by these results and by Sjöqvist's report, two patients have had this operation performed for the relief of trigeminal neuralgia.

CASE 3. (TE), A housewife, age 44, was first seen in the University of Chicago Clinics on April 11, 1938, complaining of attacks of sharp pain in the left side of the face for the past year, a dead feeling in the right leg for six years and a dead feeling in the right arm for a year. She stated that in 1932 her right leg began to feel heavy and dull. As this progressed, walking became difficult. Three years later the right hand became numb, but improved after extraction of some teeth. A few months before admission the right hand again became numb so that she was unable to hold objects in it. At times when trying to walk she became dizzy. Two years ago she had her first attack of pain in the left side of the face. It did not recur until the fall of 1937 and then lasted only a short time. About 2 weeks previous to admission it returned, occurring 2 to 3 times a day. She described the

FIG. 4. *Case 3.* To show the absence of the corneal reflex on the left side following section of the descending root of the trigeminal nerve.

FIG. 5. *Case 3.* To show the boundaries of the sensory disturbances on the left side of the face. The line indicates the limits of hypalgesia and hypothermaesthesia, the inferior interrupted line the lower limit of tactile disturbance. Below the faint line at the level of the eye the disturbances were much more severe than above.

attacks as shocks radiating from the left cheek and mandible to the midline, but never above the eye. The paroxysms of pain lasted about 10 min. and were relieved by cold packs. They were initiated by pressure on the lower teeth, washing the face, eating, etc., so that the patient was afraid to brush her teeth or wash her face. Inquiries into her systemic functions, family and personal history, were irrelevant.

Physical examination was essentially negative aside from the neurological findings. She was well-oriented, but mentally dull and rather slow in coöperating. Her cranial nerves were normal, except for a vertical nystagmus on upward gaze, and markedly diminished corneal reflexes, especially the left which was practically absent. No sensory disturbances to pin prick or cotton could be determined over the face. Audiometer tests showed a mild nerve type deafness but the caloric reactions were normal.

There was marked weakness and spasticity of the right extremities and left leg. On finger-to-nose and heel-to-knee tests a severe intention tremor developed on the right side. Rapidly alternating movements were poorly performed on the right but fairly well carried out on the left side. *Sensory* tests were difficult to evaluate owing to the patient's mental torpor. There appeared to be a marked diminution to touch, pin prick, and temperature on the right leg below the knee. Proprioception was markedly impaired in the right fingers and toes. Vibration was also impaired in the right ankle, patella, and wrist, and slightly at these points on the left side. Objects placed in the right hand were frequently not even appreciated. The *tendon reflexes* were very lively and both plantar responses were extensor. Hoffmann's sign was positive on the right side. Examination of the spinal fluid showed no abnomalities. The patient was considered to be suffering from multiple sclerosis with symptomatic tic douloureux. Because of the marked sensory changes the possibility of an extensive intramedullary spinal cord tumor was suggested. To confirm the diagnosis and at the same time relieve the pain a trigeminal tractotomy was proposed to the patient who was quite agreeable to the procedure.

On April 16, 1938, the left spinal tract of the trigeminal nerve was sectioned under nembutal and local anaesthesia. A grayish translucent area was seen in

the lower portion of the bulb, presumably a plaque of multiple sclerosis.

The patient had an uneventful recovery from the operation except for a pleuritis lasting 3 days. Following the operation the patient was quite free from pain, and much more alert and active then formerly. The neurological findings following operation were essentially the same as previously with the exception of the sensory status of the left side of the face (Fig. 4).

Sensory examination. On April 28, 1938 the sensory disturbances over the face were mapped for touch, pain, heat and cold, the boundaries marked with ink, and then the patient photographed. The area of marked impairment for pain extended over the entire left side of the face, along the lower border of the mandible, across the masseter, in the auricle, and then vertically for 3 to 4 cm. when it again extended posteriorly to the operative scar. Below the level of the eye the loss was much greater than above that level, although the changes were quite definite even on the forehead. The boundaries for cold and heat coincided with those for pain. Touch was impaired over a slightly larger area than pain. In no place was there a complete loss for any modality, and the patient could always distinguish heat and cold, and the head from the point of the pin (Fig. 5). The right *corneal reflex* was sluggish; the left absent. The masseters contracted well on both sides. There was no facial weakness (Fig. 4).

Strength of hair	Chin		Cheek		Forehead	
Touch	R.	L.	R.	L.	R.	L.
0.5 g/mm.	7	3	3	0		
1.0 "	9	6	5	2		
2.0 "	10	9	7	3		
3.0 "	10	7	10	2		
4.0 "	10	10	10	4	10	2
5.0 "	10	10	10	5		
10.0 "				7		
15.0 "			10	9		
Pin Prick						
0.125 g.	0	0	0	0		
0.5 "	5	0	4	0		
0.75 "	8	0	8	0		0
1.0 "	9	2	9	4		5
2.0 "	10	6	10	8		10
4.0 "	10	7	10	9		

Post-operative. Sensation tested by von Frey's hairs.

The patient returned *November 4, 1938,* for a check-up. She had had no pain in the face and had felt much improved over her general preoperative condition. Her legs were quite stiff, but she managed to get about with aid, and could use her hands sufficiently to cook and look after the house. Her neurological examination was essentially the same as that immediately after operation. The right corneal reflex was fairly active, the left absent. Heat, cold and pinprick were appreciated on both sides of the face, but definitely less so on the left side in about the same degree and distribution as immediately postoperatively. Deep pressure pain was markedly decreased on the left side. Two point discrimination was slightly decreased over the left cheek. Touch was said to be impaired in the same area as pain and temperature. Localization of touch on the left side of the face was also slightly defective as compared to the right side. The left side of the tongue and palate were hypaesthetic as compared to the right. The uvula lay slightly to the left of the midline at rest and deviated to the right on phonation. There was no dysphagia or dysarthria. Graduated sensory examination of the face is shown in table at top of next page.

CASE 4. (JS). A well-preserved male, age 50, was first seen in the University of Chicago Clinics on June 21, 1929, complaining of severe, paroxysmal, sharp, stinging pain in the right lower jaw during the previous 15 years. Six years before admission an alcohol injection (the exact site is unknown) gave complete relief for two and one-half years. Since that time the pain had been recurring at intervals particularly in the cold weather. It was

Strength of hair	Chin		Cheek		Forehead	
Touch	R.	L.	R.	L.	R.	L.
0.5 g./mm.	3	0	3	3	1	1
1.0	3	0	7	2	1	0
2.0	9	1	7	3	3	3
3.0	10	5	10	6	7	1
4.0	9	2	9	4	6	3
Pin prick						
0.125	0	0	0	0	0	0
0.5	3	0	2	0	4	0
0.75	6	0	7	1	7	1
1.0	6	0	8	3	9	3
2.0	7	2	8	2	6	2
4.0	8	4	9	2	9	7
6.0	9	7	10	7	10	8

initiated by eating, drafts, shaving, etc. Recently two alcohol injections failed to give relief from the pain.

His personal and family histories were irrelevant.

The patient was in excellent physical condition. The only abnormalities found on neurological examination were a slight right lower facial weakness and an area of anaesthesia along the lower right jaw.

On June 22, 1929, a right retrogasserian neurectomy was performed by Dr. Percival Bailey, the lower two-thirds of the posterior root being sectioned and the motor division spared. There resulted a complete anaesthesia of the third division and a partial anaesthesia of the second but no motor weakness of the masseter or pterygoid muscles.

About a year after the first operation he began to experience attacks of pain in the left mandibular region occurring at irregular intervals. During the last year the pain had radiated into the cheek. About three weeks before admission shooting pains were noted in the left forehead. These pains were paroxysmal and characteristically initiated by cold drafts striking the face, touching the forehead, etc. At the time of hospital admission the more severe pain was present in the forehead. Anaesthesia was present over the third division and hypaesthesia over the third division of the right trigeminal nerve. There were no sensory disturbances on the left side of the face and no weakness of the masseter or pterygoid muscles on either side. On July, 12, 1938, the left spinal tract of the trigeminal

Strength of hair	Chin		Cheek		Forehead	
Touch	R.	L.	R.	L.	R.	L.
0.5 g./mm.	very occasional response on left face only					
1.0	0	4	2	4	1	6
2.0	0	9	0	8	3	4
3.0	0	7	0	8	3	6
4.0	0	8	0	8	8	9
5.0	0	10	0	9	7	10
Pain						
0.125 g.	0	0		0	0	0
0.5	0	4	0	4	1	2
0.75	0	7	0	8	0	2
1.0	0	9	0	7	2	2
2.0	0	9	0	10	3	4
4.0	0	10	0	9	5	9
10.0	0	10	0	10	10	10

nerve was sectioned under ether anaesthesia. The patient had an uneventful recovery, but the pain in the first division was not relieved. Sensory examination showed a marked hypalgesia over the third division, less over the second and slight over the first division of the left trigeminal nerve. To give relief from the pain, the supra-orbital nerve was avulsed on July 16, 1938.

Repeated neurological examinations showed that the abnormalities were confined to the sensory status of the face. The findings using von Frey hairs before and after operation are as shown in the table at foot of page 244.

Pre-operative examination. Patient is quite coöperative.

Postoperative examinations. July 15, 1938 (1:30 p.m.). Patient coöperative but responses only fairly consistent.

Pain	L.	L.	L.
0.75 g.	1	1	5
1.0	3	2	4
2.0	1	3	9
4.0	1	(inattentive)	10
6.0	2	5	7

July 21, 1938 (3:00 p.m.) Coöperation good.

Touch	L.	L.	L.
1.0 g./mm.	0	8	0
2.0	3	10	1
3.0	4	10	1
4.0	7	10	2
5.0	8	10	1
7.5	8	10	3
10.0	10	10	1
20.0			5
Pain			
0.5 g.	0	0	0
0.75	1	1	1
1.0	1	1	1
2.0	0	1	1
4.0	0	3	0
8.0	2	0	0
10.0	1	2	0

Following operation the sensory disturbances seemed to be more severe than those in the first case as judged by the measurement by graduated stimuli. Although the patient appeared to coöperate well, his attention was readily distracted, and he fatigued easily. For this reason the objective tests are not entirely reliable. There was no doubt, however, in the minds of several observers, that there was a severe hypalgesia in the third division, a lesser hypalgesia in the second division and before avulsion of the supraorbital nerve little sensory disturbance in the first division. The appreciation of cotton wool was slightly but definitely diminished in the same areas.

Discussion

The sensory disturbances in the face after section of the spinal part of the trigeminal nerve are similar to those in the syndrome of the posterior cerebellar artery. The findings suggest that the fibers in this tract carry im-

pulses of pain and temperature and to a lesser extent touch. That touch is involved in these lesions is contrary to most of the earlier studies. Wallenberg[20] in summarizing the findings in one of his cases states that all sensory qualities were impaired but that pain and temperature were markedly reduced. Practically none of the other classical papers on the subject—Spiller[17] Gerard,[10] etc.,—suggest that touch is at all involved in these cases. This discrepancy may be explicable in one of at least three ways. The analgesia is so severe that the slight tactile disturbances may be overlooked. In most reported cases tactile sensibility was not examined by graduated stimuli, which are usually necessary to bring out the impairment. Individual variations in the tract and extent of the lesions may explain the failure of certain previous investigators using von Frey hairs to demonstrate the tactile impairment.

That, after apparently partial trigeminal tractotomy, the sensory disturbances in the face are much more pronounced in one part than in another favors the conception of Bergman,[2] van Gehuchten,[9] Davis and Haven,[6] and Sjöqvist[16] that there is a topical localization within the spinal tract of the fifth nerve. In both cases reported here the sensory disturbances were most marked over the lower part of the face, but in two of Sjöqvist's cases the analgesia was most pronounced in the first division. Because the exact site of the incision is unknown it is, of course, impossible to state from the present cases the precise topical arrangement of the spinal tract of the trigeminal nerve. The hypothesis of Bergman[2] and van Gehuchten[9] that the ophthalmic fibers lie in the ventral portion of the tract appears to be quite compatible with the present findings.

The arrangement of the sensory modalities within the spinal root of the trigeminal nerve is as yet a mystery. There is, however, ample evidence to suggest that, of the various categories of sensation carried in this tract, pain, heat, cold, pressure sense and touch are to varying degrees isolated. Several writers (Spiller,[17]; Head and Holmes,[11]; and Robinson,[14]) have reported cases of thrombosis of the posterior inferior cerebellar artery in which the appreciation of pinprick was lost, but heat and cold were undisturbed. Breuer and Marburg[3] have reported a similar case in which only the appreciation of cold was absent while pinprick and heat were appreciated. Sjöqvist[16] states that deep pressure sensibility was lost in some of his cases following trigeminal tractotomy, as it was in the first of the two cases reported here.

Summary

1. The anatomical characteristics of the spinal tract of the trigeminal nerve are discussed. Its functional divisions are correlated with its anatomical structure.

2. The sensory disturbances over the face in two cases of thrombosis of the posterior inferior cerebellar artery are presented.

3. Trigeminal tractotomy is an operation which, under exceptional con-

ditions, is indicated for the relief of trigeminal pain. The technique of the operation is discussed.

4. The sensory findings in two cases of trigeminal tractotomy are presented.

5. Analysis of the above cases and similar ones in the literature suggest that the spinal tract of the fifth nerve carries sensations of pain, heat, cold, deep pressure-pain and to a slight degree touch. These sensibilities are probably isolated to some extent in the tract.

REFERENCES

1. Bailey, P. Personal communication.
2. Bergman, E. Ueber experimentelle aufsteigende Degeneration motorischer und sensibles Hirnnerven. *Arb. neurol. Inst.* (*Anat. Physiol. Zent. Nerv.*) *Univ. Wien*, 1892, *1:* 73–97.
3. Breuer, R., and Marburg, O. Zur Klinik und Pathologie der apoplectiformen Bulbärparalyse. *Arb. neurol. Inst.* (*Anat. Physiol. Zent Nerv.*) *Univ. Wien*, 1902, *9:* 181–250.
4. Cajal, S. Ramón y. *Beitrag zum Studium der Medulla oblongata des Kleinhirns und des Ursprungs der Gehirnnerven.* Leipzig, J. A. Barth, 1896, VII, 139 pp.
5. Dandy, W. E. Certain functions of the roots and ganglia of the cranial sensory nerves. *Arch. Neurol. Psychiat., Chicago*, 1932, *27:* 22–26.
6. Davis, L., and Haven, H. A. Surgical anatomy of the sensory root of the trigeminal nerve. *Arch. Neurol. Psychiat., Chicago*, 1933, *29:* 1–15.
7. Dogliotti, M. First surgical sections, in man, of the lemniscus lateralis (pain-temperature path) at the brain stem, for the treatment of diffused rebellious pain. *Curr. Res. Anaesth.*, 1938, *17:* 143–145.
8. Gasser, H. S., and Erlanger, J. The rôle played by the sizes of the constituent fibers of a nerve trunk in determining the form of its action potential wave. *Amer. J. Physiol.*, 1927, *80:* 522–547.
9. Gehuchten, A. van. Recherches sur les voies sensitivies centrales, la voie centrale du trijumeau. *Névraxe*, 1901, *3:* 235–261.
10. Gerard, M. W. Afferent impulses of the trigeminal nerve. *Arch. Neurol. Psychiat., Chicago*, 1923, *9:* 306–338.
11. Head, H., and Holmes, G. Sensory disturbances from cerebral lesions. *Brain*, 1911, *34:* 102–254.
12. His, W. Die Entwicklung des menschlichen Rautenhirns vom Ende des ersten bis zum Beginn des dritten Monats. *Abh. sachs. Ges.* (*Akad.*) *Wiss.* 1891, *17:* 1–74.
13. Kutner, R., and Kramer, F. Sensibilitätsstörungen bei acuten und chronischen Bulbärerkrankungen. (Zugleich Beiträge zur Kenntniss der Syringobulbie.). *Arch. Psychiat. Nervenkr.*, 1907, *42:* 1002–1060.
14. Robinson, G. W. Occlusion of the posterior inferior cerebellar artery. *J. Amer. med. Ass.*, 1913, *61:* 179–180.
15. Serra, A., and Neri, V. Die elektro-chirurgische Unterbrechung der Zentralbahnen des V. Paares am lateralen ventralen Rand des Pons Varoli als erster Behandlungsversuch von hartnäckigen Neuralgien des Trigeminus durch Tumoren der Schädelbasis. *Zbl. Chir.*, 1936, *63:* 2248–2251.
16. Sjöqvist, O. Studies on pain conduction in the trigeminal nerve. *Acta psychiat. Kbh.*, 1938, *17* (Suppl.): 1–139.
17. Spiller, W. G. Remarks on the central representation of sensation. *J. nerv. ment. Dis.*, 1915, *42:* 399–418.
18. Spiller, W. G., and Frazier, C. H. The division of the sensory root of the trigeminus for the relief of tic douloureux; an experimental, pathological and clinical study, with a preliminary report of one surgically successful case. *Philad. med. J.*, 1901, *8:* 1039–1049.
19. Van Wagenen, W. P. Some indications for section of the posterior root of the trigeminal nerve through the posterior fossa. *Ann. Surg.*, 1931, *94:* 1013–1017.

20. WALLENBERG, A. Klinische Beiträge zur Diagnostik acuter Herderkrankungen des verlängerten Markes und der Brücke, *Dtsch. Z. Nervenheilk.*, 1901, *19:* 227–248.
21. WALLENBERG, A. Anatomischer Befund in einem als "Blutung in der rechte Bruckenhalfte etc. aus dem Ram. central arter, radicular u. facialis dextri" geschilderten Falle. *Dtsch. Z. Nervenhlk.*, 1904, *27:* 436–464.
22. WINDLE, W. F. The distribution and probable significance of unmyelinated nerve fibers in the trigeminal nerve of the cat. *J. comp. Neurol.*, 1926, *41:* 453–477.
23. WINDLE, W. F. (Referred to by Davis and Haven as personal communication.)
24. WINKLER, C. A case of occlusion of the arteria cerebelli posterior inferior. *Proc. Acad. Sci. Amst.* (Sect. Sci.), 1915, *17:* (2nd pt.), 914–926.

TIME CONSTANT OF EXCITATION AND VELOCITY IN SUPERNORMAL PHASE OF NERVE

H. A. BLAIR

From the Department of Physiology, School of Medicine and Dentistry, The University of Rochester, Rochester, New York

(Received for publication February 15, 1939)

THE SUPERNORMAL phase of the frog's motor nerve is often sufficiently long to permit measurement of a strength-duration curve for comparison with that of the same nerve at rest. This was first done by Adrian (1920) who concluded that the strength-duration curve of the supernormal condition differed from the normal only in that the voltage for each duration was lowered in a constant ratio. In other words, chronaxie was the same as usual during supernormality despite the lowering of the rheobase. The substantiation of Adrian's conclusion is important for at least two reasons: (i) in studying the relatively refractory period of nerve (including the supernormal phase) by means of shocks of short duration it is desirable to know what parameters of excitation should be used in expressing the divergence from normal (Blair, 1938, p. 136), and (ii) an easier method is provided for testing theories of propagation if the time constant of excitation does not vary appreciably as the velocity of the nerve impulse varies during the relatively refractory and supernormal phases. For these reasons, which will be discussed more fully later, voltage-capacity curves of the frog's sciatic nerve were measured both at rest and during the supernormal phase.

METHOD

The sciatic-nerve gastrocnemius muscle preparation was dissected and kept in the cold for at least one day before using. It was then set up in Ringer's solution in an apparatus made from a block of paraffin with the muscle in one chamber and the nerve in a small trough connecting four chambers, in each of which a stimulating lead ending in a chlorided silver wire was inserted. The upper pair of leads was connected to a stimulator consisting essentially of an 885 thyratron tube through which a 0.1μF condenser in series with 13,000 Ω could be discharged by interrupting the negative grid bias. The lower pair of leads was connected to a similar device with the same resistance but with a variable condenser enabling a voltage-capacity curve to be determined. The grid of each tube was controlled by a commutator arranged in such a way that the interval between the stimulus to the first lead and to the second could be given any desired value. In each circuit was a potentiometer in parallel with the nerve enabling the strength of the stimulus to be controlled. The circuits were sufficiently independent at the nerve so that a sub-threshold shock over one pair of leads had no observable effect on the threshold stimulus over the other. The measurements were made by determining first the normal threshold for a given capacity on the lower pair of leads, then the threshold at the end of a given interval after a maximal shock over the upper leads. Then if a voltage-capacity curve was required the procedure was repeated for other capacities, or if the supernormal phase was to be determined the procedure was repeated for other intervals. In either case the muscular response was used as an index. If the interval was short the threshold for minimal summation due to the second shock was determined or if the interval was long the threshold for a second response was observed. The speed of the commutator was such that a pair of shocks could be delivered every 8 sec.

The Ringer's solution contained: 0.65 g. Na Cl, 0.01 g. KCl, 0.015 g. Ca Cl_2, 0.192 g. $Na_2 HPO_4$ (12 H_2O) and 0.0184 g. Na H_2PO_4 (H_2O) per 100 cc.

The Supernormal Phase

Figure 1 illustrates the supernormal phase of a nerve which has been isolated for at least several hours. It is considerably exaggerated over those taken soon after dissection, both in duration, which may be a large fraction of a second, and in its maximal value, which is commonly about 35 per cent in terms of the strengths of the test shocks, or 100/65 (as it is usually expressed) in terms of excitability. Figure 1 shows that the disappearance of the supernormal state is sufficiently slow at most parts of the curve so that no great change occurs in 0.01 sec. which is as long as the utilization time of the rheobase for this tissue will ordinarily be. Therefore, the strength-duration curve taken at most phases of the supernormal state will not be markedly distorted by progressive changes of the state even with the longest stimuli.

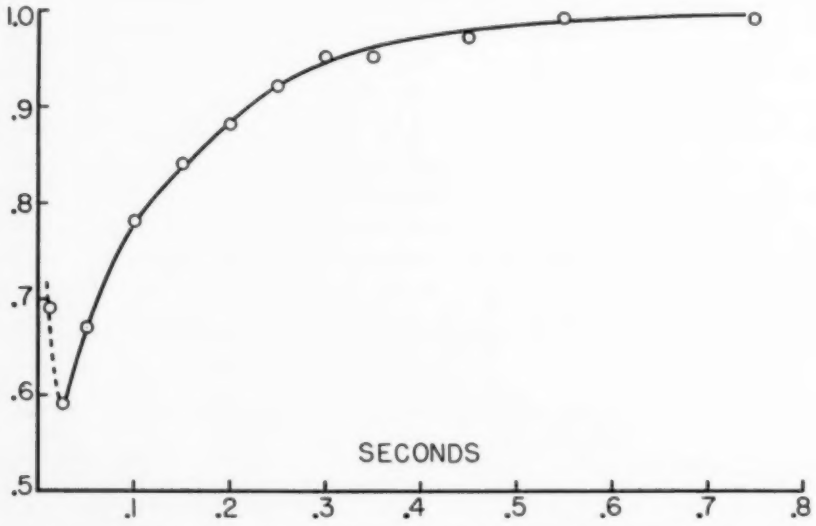

Fig. 1. Unit value of the ordinates is the normal threshold with a stimulus of time constant 0.3 msec. The ordinates of the curve are the threshold strengths of similar shocks during the supernormal phase following a maximal shock at zero time. The early part of the refractory period was not determined.

The voltage-capacity curves

In the voltage-capacity determinations, the longest stimulus used had a time constant of 13 msec. since the resistance was always 13,000 Ω and 1μF was the largest capacity. The voltage required with this capacity was close to the rheobase as is evidenced by the fact that usually the voltage had to be raised only slightly with 0.5μF. Figure 2 gives a typical comparison between voltage-capacity curves taken at rest and during the supernormal phase at 75 msec. after its beginning. Superficially there is no well defined change in chronaxie, but when the ratio of the voltages for each capacity is

determined it is found that it increases definitely as the capacities become smaller. This is illustrated in the same figure for the same data and for a number of cases in Fig. 3.

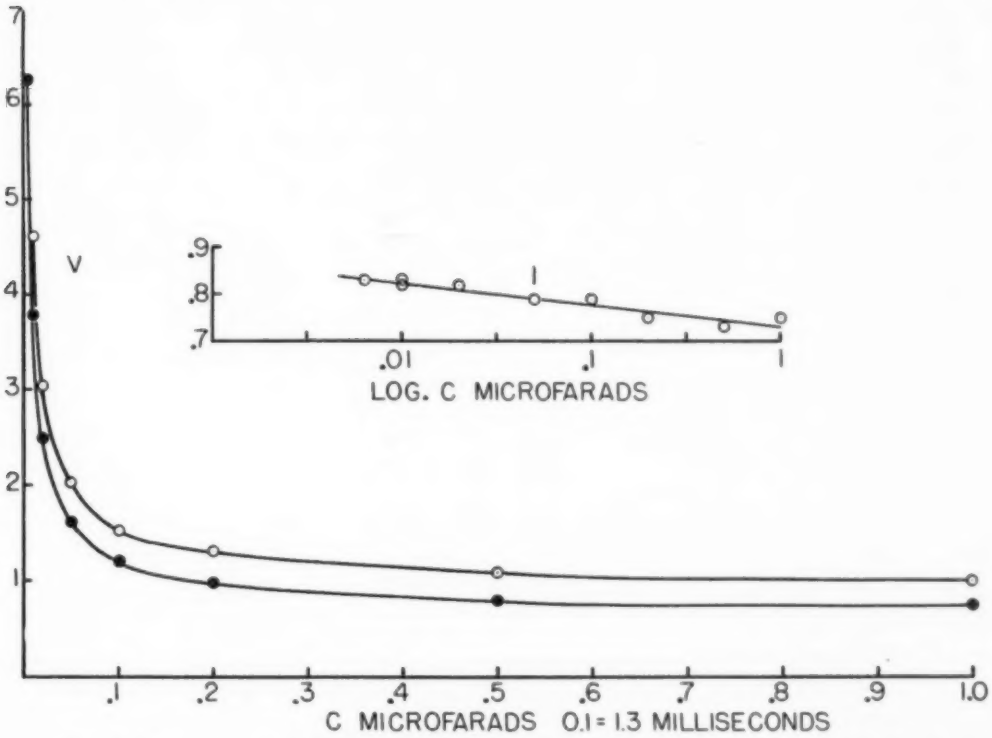

FIG. 2. The normal voltage-capacity curve (in open circles) on a scale with the rheobase equal to unity and one obtained 75 msec. after the beginning of the refractory period (in dots). The ratio of the supernormal voltage to the normal for each capacity is plotted above against the logarithm of the capacity. Chronaxie is marked by a vertical bar. The ratio increases from 0.74 to 0.79 on going from the longest stimuli back to chronaxie.

In Fig. 3, the abscissae are capacities on a logarithmic scale for convenience and the ordinates are the ratios of the voltage thresholds during the supernormal phase to those of the normal nerve at the same capacities. Each curve represents data for a different interval between the initial and test stimuli corresponding in general to a different stage of recovery. Each one is on a different nerve, however, so no relation such as that shown in Fig. 1 can be obtained from these cases. The ratio of the thresholds usually increases considerably in going from the largest to the smallest capacity and by several per cent in going from the rheobasic durations to chronaxie, which is marked by a vertical bar in each case. To answer the question how much change in the time constant of excitation is involved it is convenient to use the equation of the voltage-capacity curve.

$$\frac{V}{R} = (crk)^{1/crk-1} \qquad (1)$$

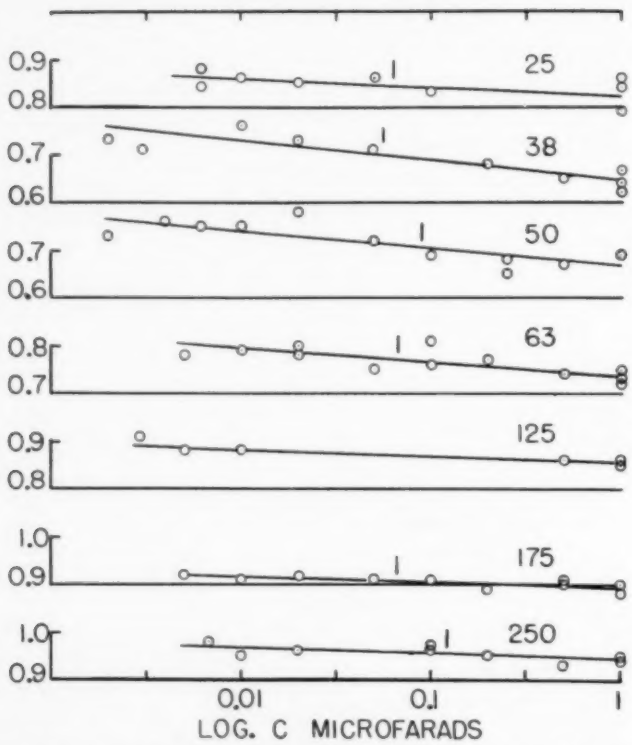

FIG. 3. The ratio of the threshold voltage during the supernormal phase to the normal against the logarithms of the capacities. The resistance of the circuit was always 13,000 Ω so 0.1μF equals 1.3 msec. The number above each curve is the time in msec. from the beginning of the refractory period. The vertical bars mark the chronaxies.

V, being the initial voltage of the condenser stimulus, R, the rheobase, and cr, the time constant of the circuit, derived from the assumptions (1) that the excitatory state E grows in response to the stimulus according to

$$\frac{dE}{dt} = KV - kE \tag{2}$$

K and k being constants, and (2) that E becomes adequate on attaining the value h (Blair, 1932). By substituting in equation (1), it will be seen that $V = 2R$ when $crk = 2$. In other words, $k = 2/\text{condenser chronaxie}$. On differentiating 1 with respect to k and putting in the condition $V = 2R$ and $crk = 2$.

$$\frac{dV}{dk} = \frac{1}{k}(2 - 4 \log_e 2) = \frac{-0.8}{k} = -0.4\,cr$$

which is the variation of V with k in the region $V = 2R$. The value of k at

20°C. is about 3000 sec.$^{-1}$ since the chronaxie, $cr = 0.7$ msec. approximately. Therefore $dV/dk = -1/3700$ approximately. Thus in fair approximation, if V, when equal to 2, changes by 0.02 or 1 per cent, k changes by $0.02 \times 3700 = 74$ or 2 per cent.

In Fig. 2, V during the supernormal phase is about 5 parts in 75 or 7 per cent larger at the chronaxie region than it would be if the excitability had not changed. Therefore, according to the argument above, k is reduced

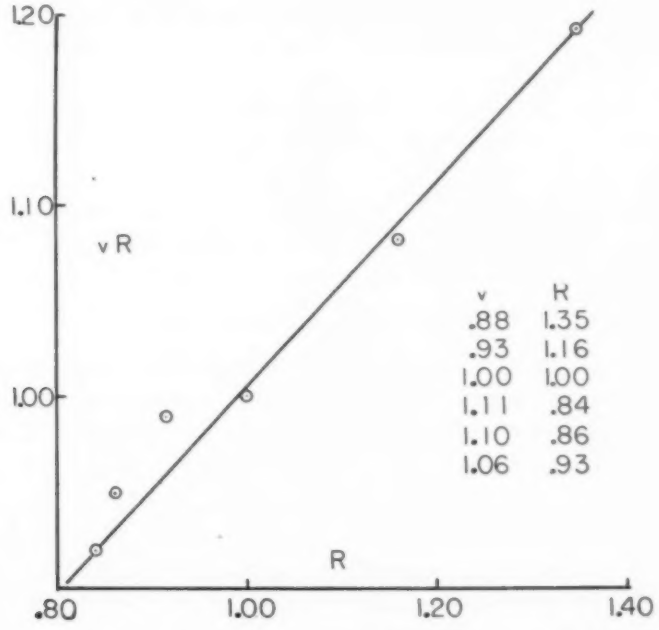

FIG. 4. The velocity v times the shock strength R plotted against R for the data inset. The normal velocity and the normal shock strength are each given the arbitrary value unity. These data of the velocity during the recovery period in frog's nerve are from a graph given by H. T. Graham, (1934, p. 234). The upper points are during the subnormal and the lower during the supernormal phase.

by about 14 per cent in this particular case, or chronaxie is similarly increased. It will be seen in Fig. 3 that k is always smaller during the supernormal phase although not by more than about 5 per cent when the recovery is sufficient to make the rheobase ratio greater than 0.85. This is the range in which most previous work has been done and Adrian's conclusion is not seriously invalid here. It will be seen, however, that the assumption of an invariable excitability is far from valid when the supernormality is large and that in consequence the form of the recovery curve depends on what type of stimulus is used to determine it, for if cr becomes so small that crk is $\ll 1$ in equation (1), $V/R = 1/crk$, but $R = kh/K$ so $crV = h/K$. There-

fore, short stimuli of constant durations measure the recovery in terms of h/K essentially, while long shocks such as the rheobase measure kh/K including changes in the excitability k as well. Most measurements of the recovery cycle have been made with short shocks enabling the phenomenon to be described in terms of h/K only. A complete description of the cycle must include also, however, the variation of k as well.

It will be observed that since $crV = h/K$ when cr is small, and $R = kh/K$, $V/R = cr/k$. Thus using subscripts 1 and 2 for the normal and supernormal conditions respectively, and assuming the same value cr for a brief stimulus in each, it will be observed that

$$\frac{V_2}{V_1} = \frac{k_1}{k_2} \times \frac{R_2}{R_1}$$

and taking for the data of Fig. 2, $V_2/V_1 = 0.83$ at $cr = 0.01$ and $R_2/R_1 = 0.73$ $k_1/k_2 = 1.14$, a result similar to that obtained above by an alternative method.

The Velocity Problem

Rashevsky (1931, 1933), using the hypothesis that the nerve excites itself electrically to effect propagation has developed a general method for expressing the velocity of the nerve impulse in terms of the parameters of excitation and the physical properties of the nerve fibre. Using the excitation law given by equation (2) this leads to the expression for the velocity v,

$$v = \frac{I - R}{R} \times \frac{k}{\alpha} \tag{3}$$

in which I is the action current, R the action current rheobase, α includes various physical properties and k is the excitability. There are difficulties in testing this expression by means of data from different fibres in a trunk because it is not known how the physical properties vary from fibre to fibre. During the recovery cycle, however, one can study the variations of the velocity in a given fibre whose physical properties and whose action current probably do not change appreciably, while the quantities R and k do. In particular, if k changes relatively little and I and α are assumed constant, there is the linear relation

$$vR = \text{constant } (I - R) \tag{4}$$

connecting the velocity and the rheobase or, which is the same thing under these conditions, the shock strength.

A set of data by Graham (1934) are plotted according to equation (4) in Fig. 4. The agreement is not bad, but since the supernormal phase is 16 per cent at the maximum, k is probably reduced by 5 per cent or more at that stage so it cannot be considered a constant. It can be seen from the

previous discussion that in putting $kh/K = R$ in the denominator of equation (3), equation (4) may be written. $vS = \text{constant} \times (I - R)$, S being the strength of a brief shock. Thus the way to correct for the effect of k being reduced in this case will be to move the lowest two points a few per cent toward the left, leaving the ordinates the same, which will not make the approximate linearity any worse.

This single result cannot be taken as substantiating Rashevsky's theory to any great extent. It is given more as an illustration of the method of testing the electrical propagation hypothesis in this way which, is relatively simple, even though the excitability k is a variable during recovery; for it is necessary, according to the equation just above, to measure only S and R at any stage of recovery in order to take the variations of k into account. There is a possible difficulty which is perhaps impossible to solve directly, namely as to whether k varies during the early, subnormal, phase of recovery. For this reason it may be necessary to confine the application of equation (4) to those parts of recovery during which the variations of k are directly measurable. The supernormal phase can be made great enough, however, to give a range of velocity variations adequate for the purpose.

Summary and Conclusions

Comparison of normal voltage capacity curves from the frog's sciatic nerve with those taken during the supernormal phase of recovery shows that the time constant of excitation is decreased (chronaxie is increased) during the supernormal phase by as much as 15 per cent when the supernormality is more than 30 per cent. Therefore a complete description of the recovery in nerve must take variations of the excitability into account as well as the other excitation parameters. Also the supernormal phase will be greater in depth, as determined by stimuli of long than of short duration, since the latter tend to ignore changes in the time constant. A method is described for testing the validity of Rashevsky's electrical self-excitation theory of nerve impulse propagation by relating the altered excitation parameters to the altered velocity during the recovery cycle. A single set of data by Graham lends support to the hypothesis.

BIBLIOGRAPHY

Adrian, E. D. The recovery process in excitable tissues. I. *J. Physiol.*, 1920, *54:* 1–31.

Blair, H. A. On the excitation of tissue by means of condenser discharges. *J. gen. Physiol.*, 1932, *16:* 177–189.

Balir, H. A. On the kinetics of recovery during the refractory period in frog's nerve. *J. Neurophysiol.*, 1938, *1:* 127–143.

Graham, H. T. Supernormality, a modification of the recovery process in nerve. *Amer. J. Physiol.*, 1934, *110:* 225–242.

Rashevsky, N. On the theory of nervous conduction. *J. gen. Physiol.*, 1931, *14:* 517–528.

Rashevsky, N. Some physico-mathematical aspects of nerve conduction. *Physics*, 1933, *4:* 341–349.